INTRODUCTION

Premature rupture of membranes (PROM) is an obstetric conundrum. It is poorly defined, has an obscure etiology, is difficult to diagnose and is associated with significant maternal, fetal and neonatal risks.

The normal development, structural integrity and function of the fetal membranes are essential for the normal progress and outcome of pregnancy. The fetal membranes insulate the fetus and amniotic fluid against microbial infections. Together with the amniotic fluid the membranes protect the fetus against blunt trauma and the umbilical cord against compression. One of the most important functions of the membranes is to remain intact until the onset of labour at term in order to maintain the protective intrauterine fluid environment; the amniotic fluid upon which the fetus depends for its survival in utero.

In most pregnancies labour begins at term in the presence of intact fetal membranes. Without interventions their spontaneous rupture usually occurs near the end of the first stage of labour. However, in 10% of pregnancies fetal membranes fail to maintain their structural integrity, resulting in their prelabour rupture.

PROM is the rupture of membranes before the onset of labor. When PROM occurs before 37 weeks of gestation it is referred to as preterm prelabour rupture of membranes **PPROM**

Latent period: the time between the rupture of membranes and delivery.

Prolonged PROM: it is the term used when >24hrs have elapsed before labor ensues. The relationship between PROM and infection has been long established. In developing countries, the incidence of lower genital tract infections during pregnancy is rather high and ranges between 40-54%. Such infections include vulvovaginitis, cervicitis, bartholinitis. infection of the birth passage is associated with changes in cervix and preterm rupture of fetal membranes.

Cigarette smoking, vaginal bleeding, previous preterm delivery, low socio-economic status, cervical incompetence, nutritional deficiencies of copper and ascorbic acid, abnormal placentation, polyhydramnios, coitus in pregnancy and multiple gestation are the risk factors for PROM.

The diagnosis of PPROM is based on history and sterile speculum examination confirming the pooling of amniotic fluid in the posterior vaginal fornix or/and direct visualization of fluid leakage from the cervical canal.

Laboratory tests such as C Reactive protein, WBC count, Gram stain of amniotic fluid, amniotic fluid culture, Interleukin-6 are useful for verifying or predicting the development of infection.

PPROM is the most common cause of preterm labour. PROM is associated with an increased risk of chorioamnionitis, unfavorable cervix and dysfunctional labor, increased cesarean rates, postpartum hemorrhage and endometritis in the mother.

The consequences of PROM for the neonate fall into 3 major overlapping categories. The first is the significant neonatal morbidity and mortality associated with prematurity. Second are the complications during labor and delivery that increase the risk for neonatal asphyxia and thirdly infection. The fetal and neonatal morbidity and mortality, risks are significantly affected by the duration between rupture of membranes and delivery and the gestational age.

Since the goal of management of PPROM is prolongation of pregnancy, the most commonly accepted management scheme for patients less than 36 weeks is expectant management, consisting of careful observation for signs of infection, labour or fetal distress in an effort to gain time for fetal growth and maturation. This expectant approach is complicated by controversies surrounding the efficacy of tocolytic agents in stopping uterine contractions, prophylactic antibiotics, corticosteroids in accelerating fetal lung maturation and amniocentesis in the diagnosis of occult infection and fetal lung maturity. In any event where

adequate facilities for intensive perinatal and neonatal care is lacking, it is prudent to refer the patient to a center where such facilities are available.

Currently most authorities accept a plan of active management which includes prevention of infection, delay of delivery until fetal maturity is achieved followed by active intervention by induction of labor.

Premature rupture of membranes is an obstetric enigma and several aspects of its management remain controversial. A careful consideration of various factors, clinical judgement and individualization of cases is necessary for appropriate management.

As the spectrum and antibiotic sensitivity pattern of etiological agents causing infections responsible for PROM and PPROM may vary from place to place, there is a need for identification of the agents and assessing the antibiotic sensitivity pattern of the organisms isolated from pregnant women coming with PROM in this area.

Hence this study is an attempt to study the risk factors for PROM, relation between vaginal infections and PROM and to assess their antibiotic sensitivity pattern. In this way the magnitude of the problem can be assessed and appropriate treatment can be instituted.

OBJECTIVES OF THE STUDY

- To identify the risk factors associated with Premature Rupture of Membranes in pregnant women.
- To culture and identify the pathogens from vaginal swabs and determine the antibiotic sensitivity in pregnant women with Premature Rupture of Membranes and in a control group.
- To associate vaginal infections with Premature Rupture of Membranes
- To record and compare the obstetric outcome among pregnant women with Premature Rupture of Membranes and in a control group.

REVIEW OF LITERATURE

DEFINITION

Spontaneous leakage of amniotic fluid prior to onset of labour.[1]

PROM has been applied to rupture of the membranes at any time before the onset of labour irrespective of the duration of gestation.[2]

The term prelabour rupture of membranes (term PROM) is defined as rupture of the membranes prior to the establishment of regular uterine contractions.[3]

Spontaneous rupture of fetal membranes occurring prior to the onset of uterine contractions, which result in progressive cervical dilation.[4]

INCIDENCE OF PROM

It is difficult to obtain an accurate determination of the incidence of PROM by reviewing the literature because of the various definitions used in establishing the diagnosis.

Spontaneous PROM occurs relatively frequently. Great difference in opinion exists between various workers regarding incidence. Its incidence varies from 2.7 to 17%. The following are a few:

Aktar and Sharma[5]- 3.3%

Killibride H.W and Thibealt[6] DW- 10%

Gunn and colleagues[7]- 2-18%

PROM is one of the most common complications occurring in about 10% of all pregnancies. It occurs in 80% of term gestation and 20% of preterm gestation. 30% of all preterm deliveries are due to PPROM and it causes 10% of all perinatal mortality.[6]

PROM without development of active labour occurs in 8% of term pregnancies (Yossef et al 2004)[8]

Duff (1996)[9] reported that PROM is a relatively common occurrence affecting 5% to 10% of pregnancies, with 60% to 80% occurring after the 37th week of gestation.

PPROM is one of the major causes of prematurity, accounting for 30-40% of all preterm births. Prematurity is an international health issue which accounts for 80% of all neonatal deaths and 60% of all juvenile neurologic handicaps.[10]

AETIOLOGY AND RISK FACTORS PREDISPOSING TO PROM

Socioeconomic status

It is not clear how socioeconomic status predisposes women to PPROM. It could be lack of access to care, different sexual hygiene habits, physical activity or other factors associated with lower socioeconomic status like stress, depression, poor general health, or nutritional deficiencies associated with unhealthy lifestyles.[11]

According to An Indian study by Karat and associates[12] the rates of PROM positively correlated with women residing in rural areas, unbooked status and coming from a lower socioeconomic background.

Body Mass Index

Several studies show that a low pre-pregnancy BMI may increase the risk for PPROM. Some investigators have suggested that BMI may be an indicator of nutritional status, although BMI fails to give any specific information about maternal micronutrient status and bioavailability of these nutrients to the fetus.

Spinillo et al[13] reported that PPROM was more strongly associated with low second to third trimester weight gain (<0.37kg per week) among women with BMI<19.5 kg/m^2 versus heavier women.

Mechanisms implicated in the pathogenesis of PROM

A number of strategies have been employed to investigate the potential mechanisms involved in PROM at the molecular, cellular, histological, biophysical and biochemical levels.

Collagen is the major structural component contributing to the strength of the fetal membranes. At the molecular level PROM appears to result from diminished collagen synthesis, altered collagen structure and accelerated collagen degradation.

1. Decrease in collagen content causes PROM. Skinner et al[14](1981) showed reduction in collagen content of amnion in PPROM cases. A decrease in type3 collagen predisposes to PPROM.
2. Increase in collagenolytic activity. Normally there is a balance between matrix metalloproteinase's (MMP) which are enzymes degrading collagen and their tissue inhibitors

which inhibit the activity of matrix metalloproteinase's. MMP-1 degrades collagen type 1,2,3 and MMP-9 degrades type 4 collagen.

Athayde et. al. (1998)[15] found an increase in amniotic fluid MMP-9 in cases with PPROM at term, in those with PPROM and in the presence of microbial invasion of the amniotic cavity.

Mc Gregor et. al. (1987)[16] found that invitro exposure to bacterial collagenase and collagenase producing microorganisms significantly reduces membrane strength and elasticity which causes the rupture of the human amniochorion in a dose dependent fashion.

An imbalance between matrix metalloproteinase (MMP) and tissue inhibitors of metalloproteinases causes PROM.

Maymon (2000)[17] showed increased amniotic fluid levels of MMP-1 in PROM.

Levels of MMP-9 increased and the levels of tissue inhibitor of MMP-1 decreased in normal labour and PROM and the imbalance between the MMPs and tissue inhibitors of MMPs may be the cause for PROM.[18]

3. Altered collagen structure. Other collagenolytic enzymes including neutrophil elastase, proteoglycanase, gelatinase and cysteine proteinase cause change in the collagen structure and in turn cause PROM.

Draper Deborah (1995)[19] found increased protease activity and increased number of different proteases in the membranes of women with PROM.

There is no evidence from biophysical testing that fetal membranes which undergo PPROM exhibit generalized weakness. A localized region of structural alteration (the zone of altered morphology) has been reported in the fetal membranes within the lower uterine segment associated with the rupture site of the fetal membranes at term (Malak et al 1994)[20].

Premature generation of the zone of altered morphology may also be a potential mechanism of PPROM. Anatomic variations of the membranes such as marginal cord insertion might constitute a local defect, reducing tolerance to stress at that site.

Relaxin is a collagenolytic peptide hormone that is produced by the corpus luteum and placenta during pregnancy in response to stimulation by human gonadotropin (hCG). Relaxin causes increased production of matrix metalloproteinases and pro inflammatory cytokines and hence has been implicated in PPROM. Placental tissues after PPROM had a significantly higher and a uniform over expression of relaxin in the placental syncytiotrophoblast. A similar group of tissues collected at term failed to show any significant differences in relaxin expression which suggests that relaxin is involved in the pathology of preterm premature rupture of fetal membranes but not in their normal rupture at term. Relaxin is over expressed in the membranes of women with PPROM (Bogic et al, 1997)[21].

Relaxin mediated pathway of PPROM is independent of infection (Millar et al, 1998)[22].

Infection and maternal response to infection in PPROM

Microorganisms can gain access to the amniotic cavity by, ascending from the vagina and cervix; hematogenous dissemination through the placenta, accidental introduction of microorganisms at the time of procedure, and by retrograde spread through the fallopian tubes. The most common pathway is believed to be the ascending pathway. In 76% of cases, microorganisms isolated from the amniotic fluid by amniocentesis are same as those from the vagina or cervix the commonest being Mycoplasma species, Streptococcus agalactiae and Streptococcus milleri (Caroll et al 1996)[23].

These organisms are also commonly associated with bacterial vaginosis, suggesting that abnormal colonization of the lower genital tract may precede the ascent of organisms from the vagina through the cervix into the uterine cavity. Bacterial lipopolysaccharides (endotoxin) in high concentration and interleukin 1 are capable of inducing production of PGE2 by amniotic epithelium, thus serving as signals for initiation of labor in the presence of maternal or intraamniotic infection.

Bacteria ascend to the membranes, cause chorioamnionitis and PROM. Bacteria cause weakening of the membranes by collagenases, proteases, elastases and by activation of the

prostaglandin cascade. These enzymes have been shown in in vitro studies to significantly reduce tensile strength and elasticity of the membranes in a dose dependent manner leading to their rupture. Activation of phospholipase -A2 enzyme by bacteria causes increased prostaglandin production, increased uterine activity causing stress on the membranes and in turn PROM.

Studies have demonstrated that exposure to fetal membranes to group B Streptococci, Staphylococcus aureus, or to activated neutrophils and neutrophil elastase resulted in significant decrease in membrane strength, elasticity and caused rupture of the membranes. Liberation of hydrogen peroxide and activation of peroxidases caused breakdown of membranes. Kovavisarach et al (2001)[24] demonstrated increased presence of Candida albicans (14.8% Vs 7.7%) and Klebsiella (7.3% Vs4.1%) in term PROM patients.

Apart from the action of bacterial enzymes and their byproducts on fetal membranes maternal response (to infection) in the form of maternal cytokines has also been implicated in the pathophysiological mechanisms of preterm labor complicated by PROM.

The most common organism isolated from maternal genital tract was Escherichia coli followed by Klebsiella. But in western countries group B Streptococci was the most common organism implicated in maternal genital tract in various studies. In a study from Delhi, the most common organism identified from maternal genital tract was Escherichia coli followed by Staphylococcus and Klebsiella. The variation of bacteria isolated from the genital tract may show regional variation of genital flora.

A study was conducted by Howard and colleagues[25] in 1984 to determine if the presence of various vaginal pathogens in early pregnancy was associated with the subsequent development of PROM or preterm labor. PROM was found significantly more often among patients with Bacteroides species and Trichomonas vaginalis.

In a study conducted by Zeng et al[26] in China, the main pathogens derived from women with PROM and their newborns were Staphylococcus and Escherichia coli, which differed from

the pathogens in Western countries. Hence, the pathogens involved in PROM should be defined in each region to maximize antibiotic effectiveness.

Subclinical infection manifested as vaginal bleeding during pregnancy could be a pathway to PPROM. Vaginal bleeding is associated with PROM especially if the bleeding occurs later in pregnancy or in more than one trimester. Subclinical bleeding is also associated with PROM and may reflect decidual dysfunction- histological evidence of subclinical hemorrhage is found in 37% of PROM deliveries compared to 8% of term controls (Salafia et al 1995[27]).

The mechanism of PROM is likely to be through activation of blood coagulation cascade. Thrombin may act upon decidual cells and through a cascade of activation of metalloproteinases and plasminogen activators leads to degradation of fetal membranes. This postulation is supported by the finding of an increased number of thrombin- anti thrombin complexes- an index of in vivo thrombin generation- in the plasma of women who subsequently proceed to PROM (Rosen et al 2001[28]).

Vaginal bleeding has been linked with PPROM as a result of release of free iron from red blood cells due to ruptured vessels and bleeding. Increased free iron has been hypothesized to catalyze the conversion of hydrogen peroxide to hydroxyl ions. Blood adjacent to chorioamnion has been hypothesized as being a medium for subclinical microbial growth.

Reactive oxygen species(ROS) are unstable molecules generated in the body which are being proposed to be responsible for damage to the chorioamniotic sac leading to their rupture. In vitro studies have shown that collagen in several tissues is the primary target for ROS. Studies linking maternal smoking, infections, antepartum bleeding, substance abuse are known to produce ROS or reduce antioxidant protection which have been hypothesized to lead to collagenolysis of the fetal membranes. Cigarette smoke contains hydrogen peroxide, superoxide, nitric oxide and hydroxyl ions which could damage the collagen matrix and consume the anti-oxidant defenses.

Cervical causes

Incompetent cervix is an important cause of PROM. There is variable evidence in literature supporting this cause and the quoted incidence is 1 in 54 to 1 in 2000 deliveries[29].

The dilated cervix in patients with cervical incompetence exposes the fetal membranes directly to the vaginal microflora and secretions, predisposing to both chorioamnionitis and PROM. Placing emergency cerclage in the presence of bulging membranes can cause PPROM.

Cervical trauma also contributes to PPROM. Common causes are forcible dilation of the cervix to >10mm, surgery to treat cervical dysplasia, and injury occurring during previous delivery. Patients with a history of multiple 1st trimester elective terminations or second trimester elective abortions are at an increased risk. Cervical dilatation with laminaria tent or cervical ripening agents, such as misoprostol, is less traumatic to the cervix than mechanical dilatation[30]. The potential residual effect of trauma to cervix due to induced abortions can be minimized by evacuation techniques and limited dilatation of cervix.

The incidence of cervical incompetence and PPROM can increase by 200 to 300 percent after preconceptual surgical treatment for CIN. The risk of subsequent preterm delivery may be proportional to the amount of cervical tissue removed during surgery. Local treatment of CIN such as laser or cold knife conization of the cervix can cause subsequent PPROM and preterm delivery[31]. Sadler and associates evaluated the association of laser conization and loop electrosurgical excision procedure with PROM. The risk of PPROM increased with the increased depth of conization[32].

A study by Evaldson et al[33] found an increased risk for PPROM in women who had increased frequencies of previous genital operations, cervical operations and lacerations. Gire et al (2002)[34] found that cervical length of less than 2cm was associated with PROM and preterm delivery.

Malpresentation

Presenting part prevents the intrauterine pressure from acting directly on the membranes by acting as a ball valve. Presenting part which ill fits as seen in malpresentations and cephalopelvic disproportion results in direct transmission of intrauterine pressure to the bag of membranes leading to its premature rupture.

Sexual intercourse

Antecedent sexual intercourse can initiate PROM by several mechanisms:

i. Seminal fluid enzymes could have a direct toxic effect on the membranes
ii. Bacteria in seminal fluid or vaginal secretion may be deposited adjacent to the cervical os in proximity to the membranes.
iii. Uterine contractions stimulated by the action of seminal prostaglandins or by orgasm can lead to preterm labour.

Diet

Deficiencies in vitamin C, copper, zinc has been associated with PPROM.
Copper plays an important role in the maturation of collagen and elastin, and it has been shown that copper deficient diet will increase fragility of supporting structures.[35]

Decreased copper levels caused decreased lysyl oxidase which is necessary for causing collagen cross links. Woods et al (2001)[36] proposed the role of deficiency of vitamin C and vitamin E in the causation of PPROM by reactive oxygen species.

Casaneuva et al[37] conducted a randomized double-blind placebo controlled trial to evaluate the effectiveness of 100 mg vitamin C per day in preventing PROM. The reported incidence was 7.69% in the supplemented group and 24.5% in the placebo group. The investigators concluded that daily supplementation with 100mg vitamin C after 20 weeks of gestation effectively reduced the incidence of PROM.

Miscellaneous

Nulliparity have been associated with PROM by some but not others. Medical conditions such as preeclampsia were noted as one of the risk factors for PPROM by Spinillo et al[38]. Anemia has been cited by some investigators as a risk factor for PPROM[39].

Invasive mid trimester procedures, such as genetic amniocentesis, fetoscopy and percutaneous umbilical blood sampling, can cause mid trimester PPROM. The risk is highest with fetoscopy. A significant obstetric history of some conditions has been associated with PPROM. Increased risk of PPROM in multifetal pregnancies has been attributed to uterine over distension creating stress in the fetal membranes leading to their rupture. A twins Study by Mercer[40] and colleagues reported an incidence of 7.4% vs. 3.7% of PPROM in twin gestation vs. singleton gestation (OR= 2.1 95% CI 1.71, 2.58).

Other factors such as coitus in late pregnancy [and] obstetric complications such as abnormal umbilical cord insertions, polyhydramnios, cervical incompetence, short cervix defined as less than 25 mm and procedures like cerclage, previous cesarean section have been associated with increased risk of PPROM[41].

Latency Period or Gestational Age at Rupture Associated with Neonatal Outcomes

Latency period is the period between membrane rupture and delivery. This period is an important clinical consideration specific to PPROM. In women with PPROM before 34 weeks, 50-60% of those conservatively managed will deliver within one week[40]. Latency period, is inversely related to the gestational age thereby increasing the risks of oligohydramnios and subsequent consequences associated with oligohydramnios.

Prolonged latency also increases the risks of ascending infection in very premature infants and their mothers. The frequency and severity of maternal and fetal complications after premature rupture of fetal membranes varies with the gestational age at rupture and delivery. Depending on when in gestation membranes rupture the decision to prolong latency or deliver may be influenced by potential neonatal outcomes. There is consistent evidence from

various studies that gestational age at preterm rupture of membranes and latency period are important independent determinants of perinatal death[42.] However, there are conflicting studies about specific neonatal outcomes associated with latency period.

DIAGNOSIS OF PROM

A combination of history, physical examination and investigations may be necessary to diagnose PROM. A history of sudden gush of liquor followed by persistent leakage is suggestive of PROM. Detailed history regarding the time of rupture, colour of the fluid and associated symptoms of uterine contractions should be noted.

A sterile speculum examination showing fluid pool in the posterior fornix and fluid emerging through the cervix provides reliable diagnosis. If the fluid is present, slight pressure on the uterus and gentle moving of the fetus may provoke leaking. If fluid is not seen the woman can be asked to perform Valsalva maneuver (cough or strain). Fluid for laboratory test should be collected over the lower blade of the speculum before it comes in contact with the vaginal wall.

The vaginal pH is acidic whereas the amniotic fluid has a pH of 7-7.5. Litmus test, Nitrazine test or Bromthymol blue test can be used to diagnose PROM. Ferning results from crystallization of sodium chloride derived from the amniotic fluid. The accuracy of the test is affected by blood or meconium.

Biochemical markers of PPROM such as fetal fibronectin, Alpha-fetoprotein and diamino oxidase should be used to confirm PPROM when the diagnosis is highly suspicious and cannot be verified by simple bedside testing.

DIAGNOSIS OF INTRAUTERINE INFECTION

Maternal WBC Count

Leucocytosis is reported in approximately 70–90% of cases of clinical chorioamnionitis. However, isolated leucocytosis in the absence of other signs or symptoms is of limited value since it may be induced by several other conditions including labor and steroid use. Therefore, routine monitoring of CBC in high-risk women (e.g., with preterm premature membrane rupture) in the absence of clinical signs of chorioamnionitis is not useful.
Elevated WBC counts signifies systemic infection but this is nonspecific.

Maternal C Reactive protein (CRP)

It is a product of hepatic acute phase reaction to infection and it is elevated in the presence of intrauterine infection. It is nonspecific marker of infection. CRP measurements during gestation remains controversial and cannot specifically predict PPROM as some studies have concluded that the CRP levels may increase with advancing normal gestation and also during labour and the postpartum period. The median CRP concentration during pregnancy ranges from 0.7 to 0.9mg/dl. Women with acute chorioamnionitis have a CRP values above 3 or 4 mg/dl and women with subclinical infection/inflammation usually exhibit values between 0.9 and 3.0mg/dl. Data show that a 30% increase in CRP levels above the base line is a promising predictor of intrauterine infection. Elevated C-reactive protein levels (at least 12 to 24 hours before delivery) were more sensitive than other standard laboratory or clinical tests in predicting chorioamnionitis both by clinical and pathologic criteria according to Ismail et al.[43]

Hawrylshyn[44] and associates found that C-reactive protein determinations were found most reliable with a high sensitivity and specificity. Elevated C-reactive protein levels correlated better with pathologic confirmation of chorioamnionitis than with the clinical febrile morbidity[44].

However, some other studies showed that the maternal serum C-reactive protein, WBC, and neutrophil counts have poor diagnostic performance for histologic chorioamnionitis[45].

The presence of both microbial invasion of the amniotic cavity (MIAC) and/or intra-amniotic inflammation was associated with the highest maternal serum CRP concentrations in a study by Musilova et al[46].

Erythrocyte sedimentation rate (ESR)

It is a nonspecific test for systemic inflammation. Elevation in the rate is seen in any type of significant infection as well as during an autoimmune disease. The levels are also increased during a normal pregnancy. Hawrylyshyn et al 1983[44] found an ESR > 60mm/hour to be very specific (100%) but moderately sensitive (65%) for histological chorioamnionitis. The lack of sensitivity limits the clinical usefulness of this test.

Maternal serum Interleukin 6 (IL-6) and Interleukin 8 (IL-8) concentration

Interleukins 6 and 8 are specific for infection and are released early in the inflammatory response. Murtha et al[47] showed that interleukin-6 concentration >8pg/ml had a positive predictive value of 96% and Negative predictive value of 98% in diagnosing intrauterine infection.

IL-6 in cervical secretions has also been investigated independently to determine its value in diagnosing microbial invasion of amniotic fluid in patients with PPROM. An IL-6 level in cervical secretions >200 pg/ml had a sensitivity of 78.5% and a specificity of 73.1% and a relative risk of 4.6 for intra amniotic infection. The study concluded that intra amniotic infection is associated with increased levels of IL-6 and concentrations in cervical secretions are related to amniotic levels.

AMNIOTIC FLUID EXAMINATION:

Culture

Culture of amniotic fluid is the most reliable test but is of limited utility since culture results may not be available for up to 3 days. In addition, because of the invasive nature of the procedure, amniocentesis is not performed in the majority of cases, which occur during labor. Amniocentesis is also used in some centers to identify subclinical chorioamnionitis in women

with spontaneous preterm labor and preterm membrane rupture at early gestational ages. However, the value of this practice has recently been questioned.

Gram Stain

Gram stain of amniotic fluid is valuable for confirming the diagnosis of amnionitis. if the gram stain is negative for both bacteria and white cells the probability of infection is less than 5%.

Glucose Concentration

Low amniotic fluid glucose concentration is another sign of amniotic infection. This is because of the metabolism of glucose by microorganisms.

WBC Count

Yoon bo hyun et al 1996[48] compared CRP, maternal WBC count and amniotic fluid WBC count and found amniotic fluid WBC count to be the best predictor for diagnosing histological and clinical chorioamnionitis and neonatal morbidity.

COMPLICATIONS OF PROM

MATERNAL:

1) **Chorioamnionitis**

- Acute
- Subclinical

Chorioamnionitis or intraamniotic infection is an inflammation of the amniotic fluid, membranes, placenta, and/or decidua. The risk of clinical chorioamnionitis increases with increasing duration of the membrane rupture, and decreases with advancing gestational age at PROM. Acute chorioamnionitis complicates 0.5 to 10% of all pregnancies but the incidence may be as high as 3-25% in pregnancies complicated by PROM of more than 24hrs duration.[49]

Diagnosis of chorioamnionitis: diagnosis can be made histologically but is generally diagnosed clinically based on the finding of:

fever (>37.8˚C or 100.4 F) and two or more of:

- Maternal pulse >100 beats per minute
- Fetal heart rate>160 beats per minute
- Foul smelling amniotic fluid
- Uterine tenderness
- Maternal Leukocytosis>15,000 cells/mm^3

Given that under-diagnosis is possible, providers should be more vigilant about diagnosing and treating chorioamnionitis in these women in subsequent pregnancies.

Women who had chorioamnionitis in their first delivery were 3.43 times as likely to have chorioamnionitis in their second delivery. [50]

Subclinical Chorioamnionitis:

On many occasions the only symptom of chorioamnionitic infection is the presence of uterine contractions. Other signs of subclinical infection are a change from a reactive to the non-reactive pattern in the Non Stress Test and absence of respiratory movements in the biophysical profile.

2) Sepsis

The patients may have endometritis, parametritis, pyelonephritis. Occasionally uncontrolled infection may lead to septicemia, DIC, shock, adult RDS and maternal mortality.

Seaward et al(1997)[51] evaluated the predictors of clinical chorioamnionitis and postpartum fever in patients with PROM and said that increased number of digital vaginal examinations, longer duration of active labour and meconium staining of amniotic fluid were important risk factors for development of chorioamnionitis and the risk factors for development of postpartum fever were clinical chorioamnionitis, increased duration of labour and cesarean section.

3) Abruptio Placenta

The reason for the high incidence of abruption in patients with PROM is the progressive decrease in intrauterine surface area causing placental detachment.

4) Oligohydramnios

When PROM is managed conservatively most patients have oligohydramnios due to continuous leakage of amniotic fluid. pregnancies complicated by oligohydramnios may have increased incidence of fetal skeletal deformities, growth retardation, pulmonary hypoplasia, fetal distress and increased need for cesarean section.

5) Retained Placenta and Postpartum Hemorrhage

they are more frequent in women with PROM than in those without PROM. This may be due to increased incidence of marginal cord insertion and battledore placenta.

6) Failed Induction and Increased Need for Operative Delivery

Pandey Swathi et al (2000)[52] in a study showed 31% incidence of cesarean section mainly due to failed induction and fetal distress.

FETAL COMPLICATIONS

1) **Prematurity**

Prematurity is the most significant risk factor for the increased perinatal morbidity and mortality associated with PPROM because delivery occurs within 7 days of PPROM in over 80% of cases.

2) **Neonatal Sepsis**

The incidence of fetal and neonatal sepsis is small, 2% to 4% with the rate correlating directly with the length of time the membranes are ruptured and the gestational age. If an intraamniotic infection develops the fetus has a 15% to 20% risk for developing septicemia, pneumonia or a urinary tract infection.

Neonatal sepsis can be divided into two main types (early onset and late onset) depending on whether the onset is during the first 72 hours of life or later. Early onset septicemia is caused by organisms prevalent in the genital tract or in the labor rooms and operation theatre. Organisms responsible include group B Streptococcus, gram negative organisms (E-coli, Klebsiella, Enterobacter). Majority of cases manifest as respiratory distress due to intrauterine pneumonia.

Early onset bacterial infections occur either due to ascending infection following rupture of membranes or during passage of baby through infected birth canal or at the time of resuscitation in the labor room.

Late onset septicemia is acquired as a nosocomial infection from the nursery or wards. The onset is delayed for 48-72 hours after birth. About two third of the cases are caused by gram negative bacilli (Klebsiella, Enterobacter, E coli, Pseudomonas aeruginosa, Salmonella typhimurium, Proteus) while the rest are contributed by gram positive organisms including Staphylococcus aureus.

Early onset sepsis is characterized by perinatal hypoxia, resuscitation difficulties and evidence of congenital pneumonia in the form of respiratory distress. The clinical presentation of late onset sepsis may be silent in a very small baby who may suddenly die without exhibiting any signs or symptoms.

3)Pulmonary Hypoplasia

This complication is frequent when PROM occurs before 26 weeks and the latent period is prolonged. It is characterized by severe respiratory distress, requiring maximal ventilator support and occurring immediately after birth. The lack of surfactant due to immaturity of lungs results in Hyaline Membrane disease. The clinical triad of tachypnoea, expiratory grunt and inspiratory retractions in a prematurely born asphyxiated infant suggests Hyaline membrane disease. The symptom may begin at birth or within 6 hours of birth and there is gradual worsening of retractions, grunting and cyanosis during the next 24-48 hours. The data from Mercer (2003)[40] show that at all gestational ages, the risk of respiratory distress is greater than risk of infection. At 24 weeks, 100% of newborns will have respiratory distress syndrome (RDS). At 28 weeks, the incidence of RDS is 85%, at 32 weeks is 25% and at 34 weeks it is close to 10%.

4)Deformities

Facial and skeletal deformities may occur as consequences of prolonged PROM due to severe oligohydramnios. With the lack of fluid, the fetus loses the protective cushion against compression and has severe limitation in the ability to move the limbs, which predisposes to the deformities. Most of these cases occur with PROM before 26 weeks and after a latency period of 5 or more weeks (Nimrod et al[53]). Since PPROM is directly associated with oligohydramnios certain fetal conditions are more likely with PPROM than other subtypes of preterm delivery. Pulmonary hypoplasia, fetal infection after membrane rupture, and fetal joint contractures due to oligohydramnios are specific consequences of PPROM. Prevention of PPROM will reduce incidence of long term morbidities associated with these conditions. In a study (Berkowitz et al, 1976)[54], 4 out of 20 non RDS deaths following PPROM were caused by congenital malformations.

5)Perinatal Asphyxia, Fetal Distress and Low Apgar Score

Various mechanisms predispose to perinatal asphyxia following PROM. They include:

1) Compression or prolapsed of umbilical cord.
2) malpresentations
3) fetal compromise following maternal fever and chorioamnionitis

Maternal fever with or without signs of chorioamnionitis has been observed to have high association with still births. Fever produces fetal asphyxia by reducing placental blood flow due to vasculitis.

The APGAR scores were low from 10.8% in non-infected to 30.3% in infected ones following prolonged PROM. Incidence of meconium staining in PROM is 3%. Neonatal encephalopathy following severe birth asphyxia or perinatal hypoxia is referred to as Hypoxic Ischemic Encephalopathy.

Neonatal morbidity is increased due to mechanical difficulties encountered with delivery (either by vaginal or abdominal route) as a result of increased incidence of malpresentation and oligohydramnios.

6) Cerebral Palsy

Cerebral Palsy is a long term sequela of PPROM, particularly in cases complicated by acute or subclinical chorioamnionitis, severe intraventricular bleeding, or intrapartum fetal acidosis and hypoxia.

CONTROVERSIES IN THE MANAGEMENT OF PROM

ROLE OF STEROIDS

Respiratory distress syndrome is a leading cause of death in the presence of PPROM. Occurrence of intraventricular hemorrhage is an added threat. Despite improvements in neonatal survival by mechanical ventilation and exogenous artificial surfactant, the goal of therapy ideally is prevention rather than treatment of respiratory disease.

Corticosteroids increase the production of surfactant phospholipids and proteins by type 2 pneumocytes. Additionally, there is some evidence that corticosteroids also accelerate structural development of pulmonary tissue (Ballart et al 1995). Their beneficial effect though proved is associated with the fear of infection.

Lewis and colleagues (1996)[55] showed 44% decrease in respiratory distress syndrome at < 30 weeks gestational age whereas Crowley (1992) showed 49% decrease in the respiratory distress syndrome incidence with the use of steroids.

Ohlsson and associated (1989) found no increase in chorioamnionitis or neonatal sepsis with antenatal steroids, but noted an increase in the incidence of postpartum endometritis.

Veremillion et al (2000)[56] used steroids at 24-32 weeks of gestational age with PROM and showed a decreased incidence of respiratory distress syndrome and intraventricular hemorrhage without increase in perinatal infectious morbidity.

DOSE of steroid: ACOG committee recommendation (2016)

dexamethasone 4 doses 6 mg/dose at 12-hour interval or betamethasone 2 doses 12 mg/dose at 24-hour interval

ACOG 2016[57] recommends:

- A single course of corticosteroids between 24 0/7 and 33 6/7 weeks, including women with PROM and/or multiple gestations, and possibly beginning at 23 0/7 weeks if at risk for delivery within 7 days, considering a family's decision.

- A single course of betamethasone between 34 0/7 weeks and 36 6/7 weeks for women at risk for preterm birth within 7 days who have not received previous corticosteroids.
- A single repeat course for certain women less than 34 0/7 weeks with risk for delivery within the next 7 days and previous corticosteroids more than 14 days earlier, and in some cases as early as 7 days from the prior dose
- The is insufficient evidence to recommend for or against a repeat or rescue dose of corticosteroids in patients with PROM.

NIH Consensus panel[58] conclusion on the use of corticosteroids

- International data support strongly the use and efficacy of a single course of steroid.
- Data insufficient to support use of repeat rescue courses.
- Repeat courses should be limited for clinical trials.

Thus, the beneficial role of corticosteroids has been proven without any doubt and beneficial effects outweigh the risks.

ROLE OF TOCOLYSIS IN PPROM

The use of tocolysis in PPROM remains controversial especially when one considers that PROM itself may be due to underlying sub clinical infection. Tocolytics are used in the presence of PPROM to forestall delivery for a short period to permit the action of steroids on the lungs. Tocolysis may also have a role to play where an in-utero transfer to a unit with neonatal care becomes necessary. Long term prophylactic tocolytic therapy in patients with PPROM may result in increased risk of maternal infectious morbidity, and raise in cost of treatment with no demonstrable benefit. Fontenot and Lewis (2001)[59] concluded that tocolytic therapy continues to be a controversial issue and though there may be some short term neonatal benefit, further investigation is warranted

Present recommendation of the use of tocolytics is for 24-48 hours till the action of steroids. Contraindication for the action of tocolytics includes chorioamnionitis, heavy vaginal bleeding, preeclampsia or eclampsia and severe fetal growth restriction.

ROLE OF ANTIBIOTICS IN PROM

Infection plays a major role in PROM, being either a cause or consequence of it and is associated with maternal and neonatal morbidity. In patients with PROM there are two rationales for prophylactic antibiotics. Firstly, for prevention of perinatal group B streptococcal infection. Secondly, antibiotic prophylaxis has been based on the hypothesis that infection is the triggering cause of PROM or the infection that ensues after PROM triggers labour. This rationale for antibiotic prophylaxis has been to delay delivery after PPROM rather than to prevent clinically evident infection. The benefits of antibiotic prophylaxis were a significant delay in delivery within 7 days, a reduction in chorioamnionitis, postpartum infection and neonatal sepsis. Antibiotics may cause allergic reactions, overgrowth of commensals and growth of resistant pathogens.

Mc Graegor et al[16] randomized 55 women with PROM to receive erythromycin or placebo and found prolonged latency and decreased neonatal hospital stay in the erythromycin group. Mercer and Arheart (1995) demonstrated that antibiotic treatment was associated with longer latency periods, reduced incidence of endometritis and less neonatal sepsis.

Mercer et al (1995) in a meta-analysis demonstrated that antibiotic treatment after PROM reduces the incidence of women delivering within one week (62% Vs 76%) as well as maternal morbidity including chorioamnionitis (12% Vs 23%), postpartum infection (8% Vs 12%) and neonatal sepsis (5.1% Vs8.7%).

Flenandy V King (2002)[60] showed decrease in chorioamnionitis and endometritis with antibiotics in PROM at term.

In women with latency longer than 12 hours, prophylactic antibiotics are associated with significantly lower rates of chorioamnionitis by 51% and endometritis by 88%.[61]

The ORACLE I randomized trial (2001)[62] attempted to cross over the question of the value of prophylactic antibiotics by randomly assigning women with PPROM to the following groups, oral erythromycin, combination of oral amoxycillin & clavulanic acid, or both or placebo. The primary outcome was a composite of neonatal death, chronic lung disease and major cerebral abnormality on ultrasound before discharge from the hospital. Analysis was by

intention to treat. Among the 2415 infants born to women allocated erythromycin only or placebo, fewer in the erythromycin only group had the primary composite outcome. Co-amoxicillin clavulanic acid alone and Co-amoxicillin clavulanic acid + erythromycin group had no benefit over the placebo group. Use of erythromycin was associated with prolongation of pregnancy, reduction in need for neonatal treatment with surfactant, decrease in oxygen dependence at 28 days of age and older, fewer major cerebral abnormalities on ultrasound and fewer positive blood cultures. The authors concluded that treatment with erythromycin was associated with the best range of health benefits for the neonate and suggested that there may be a reduction in childhood disability.

MANAGEMENT OF PROM

Prepregnancy counselling has limited role in management of PPROM because in vast majority of cases, the cause is unknown.

Recurrence risk of PPROM was studied by Naeye et al[63] who reported a recurrence rate of 21-32% and it was subsequently confirmed by Asrat and associates.[64] More recently, a lower recurrence rate of 10.7% has been reported by Lee and associates[65] , however in their study, after one pregnancy complicated by PPROM, the subsequent overall preterm delivery rate in next pregnancy was 34.2%.

A detailed examination of etiologic associations of PPROM by Harger and associates suggested that only independent risk factor that might be amenable to pre-pregnancy intervention was smoking and the risk appeared to be closely related. Other less constant associations that might be amenable to intervention include cocaine abuse, intrauterine diethylstilbestrol(DES) exposed women and possibly nutritional deficiencies of ascorbic acid, copper, zinc and iron. However, evidence that implementing interventional strategies improve outcome is lacking.

There is substantial direct and indirect evidence that reproductive tract infections and associated inflammatory changes are responsible for many instances of PPROM. Group B Streptococcus, Chlamydia, Gonococcus, Treponema, Mycoplasma hominis, Ureaplasma urealyticum have all been variously incriminated, but the value of prophylactic antibiotics is

not proven. Three studies (Gibbs and associates)[66] reported 66-70% decreased incidence of PPROM after prophylactic treatment of bacterial vaginosis in high risk women during pregnancy. Cochrane systematic review concluded that antibiotics are associated with delay in delivery and reduction in markers of neonatal morbidity. The multinational ORACLE trial showed a benefit only for the use of erythromycin in the presence of ruptured membranes.

In the light of the foregoing information, pre-pregnancy vaginal cultures would appear useful in women with a past history of PPROM especially in relation to the detection of group B Streptococcus and bacterial vaginosis.

APPROACH TO MANAGEMENT

The overall approach to management of PPROM takes into account neonatal survival at the gestational age when rupture occurs.

There are three main approaches in the management of PROM.

1. Expectant management
2. Active management
3. Aggressive management

Expectant management

Expectant management involves hospitalization and continued clinical observation of the mother and fetus. Informed consent should be obtained after counseling the parents. The role of bed rest is controversial but may aid in diagnosis by allowing a pool of amniotic fluid to collect in posterior fornix, maternal activity also seems to increase rate of fluid leakage. Specialized assessment of fetal well-being using cardiotocography, biophysical profile and obstetric ultrasonographic evaluation of fetal growth, is done periodically.

Detection of subclinical chorioamnionitis using serial WBC count and CRP estimates in association with vaginal microbiologic cultures has been advocated. NST and BPP score correlate closely with intra uterine sepsis. These noninvasive tests have obvious advantage over amniocentesis.

Active management

Active management may be defined as the expectant management plus the use of one or more of the following pharmacological agents.

- Antenatal corticosteroids
- Tocolysis
- Prophylactic antibiotic administration

Aggressive management

Aggressive management is employed when delivery is deemed necessary as a result of obstetric indication; such as fetal distress, maternal sepsis or abruption placenta or is requested by parents in the face of marked immaturity (less than 24 weeks) or demonstrated fetal maturity (after 34 weeks). Aggressive approach is based on fear of infection, consists of delivery within 24-48 hours of membrane rupture.

Identification of patients who require immediate delivery:

This is the first step in management of PROM. Such patients are:

1. Patients in labour
2. Patients with mature fetal lungs
3. Patients with fetal malformation
4. Patients with fetal distress
5. Patients with overt infection
6. Patients with subclinical amnionitis
7. Patients at high risk of infection

Determination of gestational age

Once conditions indicating the need for immediate delivery have been ruled out, gestational age becomes the most important variable in the management of PROM.

PPROM BEFORE 24 WEEKS

The perinatal outcome of PPROM before 24 weeks of gestation is extremely poor. The most appropriate management at this gestational age is not clear and must be individualized. 48% of these patients will deliver within 3 days, 67% within 1 week and 83% within 2 weeks of PPROM (Moretti and Sibai, 1988[67]).

Xiao et al (2000)[68] showed a mortality rate of 43% in PROM at < 25 weeks of gestational age, major cause of death being respiratory failure and neurological complications**.**

PPROM BETWEEN 24 AND 32 WEEKS

Pulmonary complications and infections are common with PPROM at this gestational age. The predominant risk is RDS usually due to Hyaline membrane disease affecting 30-100%. Other frequent morbidities are sepsis, affecting 10-50%, Intraventricular Hemorrhage affecting 5-50%, necrotizing enterocolitis affecting 1-10% and chronic lung disease, affecting 2 and 80%.

The obstetrical management of these women should be directed towards prolongation of the latent phase and prevention of the above complications. The antibiotics administered should be effective against Group B Streptococci and Escherichia coli and additional antibiotics should be added if the cultures obtained on admission reveal Chlamydia or Neisseria gonorrhea. A commonly used regimen is cefazolin 2 g intravenous every 8 hours for 48 hours followed by cephalexin 250 mg orally for 5 more days. However recent evidence suggests that results are similar with or without the additional 5 days of oral antibiotic therapy (Segal et al,2002[69])

PPROM BETWEEN 32 AND 36 WEEKS

Approximately 50% of the fetuses of women with PPROM between 32 and 36 weeks of gestation will have adequate lung maturity. Since the issue of fetal lung maturity is important in the management, a decisive effort should be made to collect amniotic fluid for lung maturity testing. Spinnato et al (1987)[70] found significantly increased maternal infectious morbidity and no neonatal advantages by prolongation of pregnancy in this group of women. Mercer et al (1993)[71] did a randomized controlled trial of women with PPROM between 32 and 36 weeks and with mature amniotic fluid and found increased frequency of

chorioamnionitis, prolonged maternal and neonatal hospitalization and more frequent and prolonged antimicrobial therapy in the neonates of women in the expectant management arm of the study.

Expectant management should not be adopted blindly for all women with PPROM and unknown fetal lung maturity. immediate induction and delivery or treatment with steroids and antibiotics and delivery 24 hours after the last steroid injection may be best options under the following circumstances.

1. Leukocytosis greater than 16,000 cells/mm^3 with CRP greater than 0.9 mg/dl and no bacteria in the amniotic fluid gram stain.
2. Severe oligohydramnios with the largest pocket of fluid less than 2 cm in diameter.
3. Variable decelerations and poor variability in the FHR tracing.
4. Cervical length by ultrasound less than 1.5cm with funneling
5. Cervical dilatation equal to or greater than 5cm and effacement equal to or greater than 80%.

If none of these conditions are present, management may be expectant. The women should remain in the hospital until delivery. Antibiotics should be given IV for 48-72 hours and then orally for 5 days. Electronic fetal heart rate monitoring should be performed once or twice daily.

PPROM AT 36 OR MORE WEEKS

Women with PROM after 36 weeks should be delivered as the fetal pulmonary maturity is complete or is almost complete. Induction with intravenous oxytocin is probably necessary if the cervix is effaced 75% or more and dilated 2 cm or more. Lesser degrees of cervical ripening should be managed with endo-vaginal prostaglandins. Waiting for spontaneous onset of labor for 24 hours usually does not result in maternal and neonatal infection.

Maternal temperature should be obtained frequently, the baby should be monitored by NST twice daily and ampicillin 2 g Intravenous every 6 hours or cefazolin 2g Intravenous every 8 hours should be given for the prevention of infections with Group B Streptococci and Escherichia coli. If patient is allergic to penicillin, then gentamycin 120 mg Intravenous

initial dose followed by 80 mg Intravenous every 8 hours plus clindamycin 900 mg Intravenous every 8 hours can be given. If labor does not start spontaneously within 24 hours of rupture, labor should be induced.

NEWER METHODS IN THE MANAGEMENT OF PROM

AMNIOINFUSION

De Santis and colleagues[72] studied the efficacy of trans abdominal amnioinfusion in patients with PPROM and severe oligohydramnios at less than 26 weeks gestational age. Saline amnioinfusion was first given 7 days after PPROM and repeated at weekly intervals if oligohydramnios persisted. Saline was infused into the amniotic cavity until the Amniotic fluid index (AFI) exceeded 10 cm. The latency period was longer and the gestational week of delivery was later in treated patients. Also, neonatal weight and chance of intrauterine fetal survival was also higher. Infectious complications were less frequent in women receiving amnioinfusion. There was no difference in the perinatal mortality rate and the cause of death. These findings suggest that amnioinfusion is a low risk procedure that could lengthen intrauterine fetal stay.

AMNIOPATCH

Quintero and colleagues[73] showed that the amniotic cavity could be sealed with an intraamniotic injection of platelets and cryoprecipitate and that the pregnancy might continue uneventfully thereafter. A defect ranging from 0.72 mm to 3 mm could be sealed off and thus the procedure is applicable to amniocentesis or more invasive procedures such as skin biopsy, fetal shunts or diagnostic or operative fetoscopy. The knowledge of the site of rupture was not necessary for the amniopatch, the material seemed to find its way to the defect and seal it. The precise mechanism by which the amniopatch works is unknown. Presumably platelets activation at the site of rupture and fibrin formation would initiate the healing process and allow the membrane to seal.

The amniopatch may work with iatrogenic PPROM but not in spontaneous PPROM. Potentially the location of the defect over the internal os as well as the presence of inflammation or infection or other pathological process in spontaneous PPROM may interfere

with the healing. In case of iatrogenic PPROM, the location of defect away from the os and the lack of additional pathological process may allow the healing to take place with the assistance of a platelet plug.

Although the appropriate dose of platelets and cryoprecipitate needs to be established, with amniopatch, iatrogenic PPROM may no longer be considered a devastating complication of pregnancy.

MATERIAL AND METHODS

- Study setting: labor room, antenatal and postnatal wards and neonatal ICU
- Study Design: case control study.
- Study period: December 2015 to June 2017
- Sample size: 100 cases and 100 controls

Sample size was estimated based on the difference in proportion of vaginal infections in PROM (48.75%) and in Non- PROM subjects (8.75%). By using the formula

$$\text{Sample size} = \frac{r+1}{r}\frac{(p^*)(1-p^*)(Z_\beta + Z_{\alpha/2})^2}{(p_1 - p_2)^2}$$

r = Ratio of control to cases, 1 for equal number of case and control
p^* = Average proportion exposed = proportion of exposed cases + proportion of control exposed/2
Z_β = Standard normal variate for power = for 80% power it is 0.84 and for 90% value is 1.28. Researcher has to select power for the study.
$Z_{\alpha/2}$ = Standard normal variate for level of significance as mentioned in previous section.
$p_1 - p_2$ = Effect size or different in proportion expected based on previous studies. p_1 is proportion in cases and p_2 is proportion in control.

From the Study by M Bharathi et al[74] p1 = 48.75%, p2 = 8.75% at 99% confidence level and 99% power, with equal ratio of cases and controls.

P* = 48.75 + 8.75 / 2 = 28.75% or 0.2875

1 – P* = 71.25% or 0.7125. The minimum calculated sample size was 61.

Inclusion criteria:

- Cases were Pregnant women with gestational age > 28 weeks presenting with PROM.
- Controls were pregnant women >28 weeks without PROM
- Cases and controls were matched for gestational age.

Exclusion Criteria:

- Women in active labour.

Method of Collection of Data

- Informed consent
- General physical and systemic examination, clinically relevant investigations were done.
- A questionnaire was used to collect the clinical data.
- Patients were followed up through their delivery and immediate postnatal period.

Method of Sample Collection:

- under aseptic precautions using sterile swabs 3 high vaginal swab were taken from the subjects and processed.

Processing of Samples:

- Among the 3 swabs collected, one was used for preparation of smear for gram staining.
- Second swab for culture on blood agar, chocolate agar, MacConkey agar and Sabouraud's dextrose agar was used as necessary.
- Third swab was for inoculation into thioglycollate broth.
- Bacterial isolates were identified by standard bacteriological procedures[75]
- Antibiotic sensitivity of the isolates was done by Kirby Bauer disc diffusion method according to CLSI guidelines.[76]

STATISTICAL ANALYSIS

- Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. **Chi-square test** was used as test of significance for qualitative data.
- Continuous data was represented as mean and standard deviation. **Independent t test or Mann Whitney U test** was used as test of significance to identify the mean difference between two quantitative variables and qualitative variables respectively.

- **Graphical representation of data:** MS Excel and MS word were used to obtain various types of graphs such as bar diagram, Pie diagram and Scatter plots.
- **p value** (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests.
- **Statistical software:** MS Excel**,** SPSS version 22 **(**IBM SPSS Statistics, Somers NY, USA) was used to analyze data. EPI Info (CDC Atlanta), Open Epi, Med calc and Medley's desktop were used to estimate sample size and reference management in the study.

RESULTS

Table 1: Age distribution among cases and controls (n=100 in each group)

Age(years)	Group	
	Cases (%)	Controls (%)
<20	2(2)	0(0)
20 to 25	56(56)	68(68)
26 to 30	34(34)	28(28)
>30	8(8)	4(4)

$\chi 2 = 5.075$, df = 3, p = 0.166

In the study majority of subjects in both the groups were in the age group 20 to 25 years (first half of 3rd decade). There was no statistical difference for the difference in the age groups between cases and controls.

Graph 1: Age distribution among cases and controls

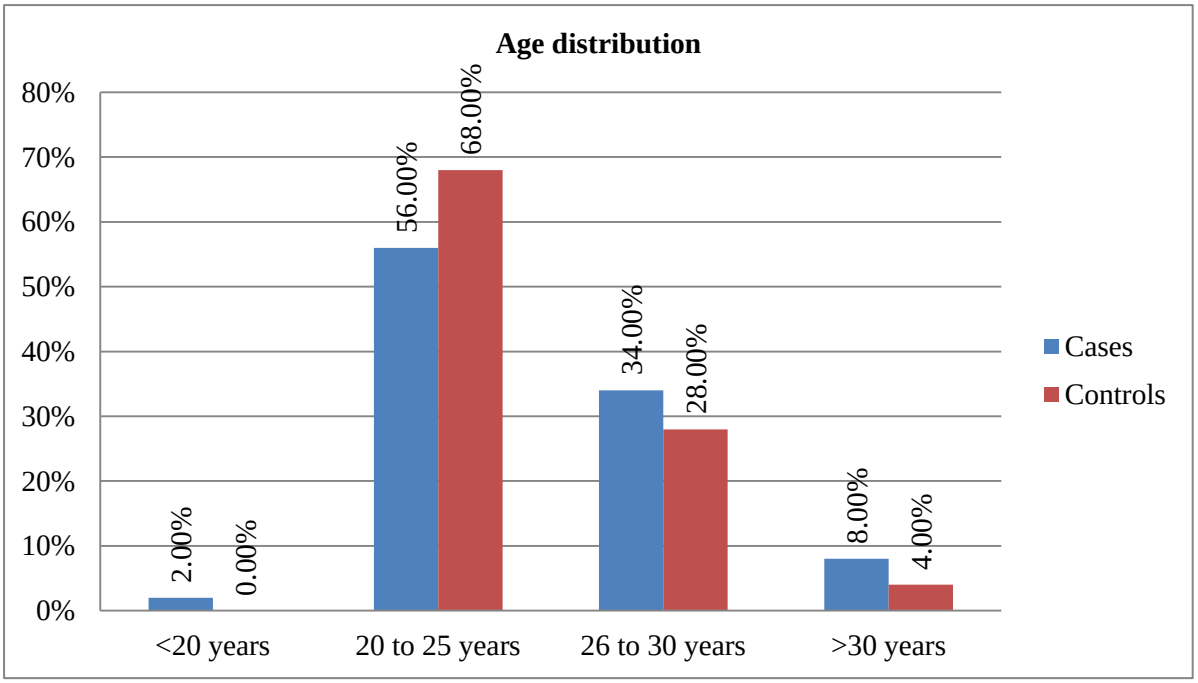

Table 2: Booking status among cases and controls (n=100 in each group)

Booking status	Group	
	Cases (%)	Controls (%)
Booked	78(78%)	89(89%)
Unbooked	22(22%)	11(11%)

$\chi 2 = 4.391$, df = 1, p = 0.036*

22% of cases and 11% among controls were unbooked patients, the difference of which was found to be statistically significant.

graph 2: Booking status among cases and controls

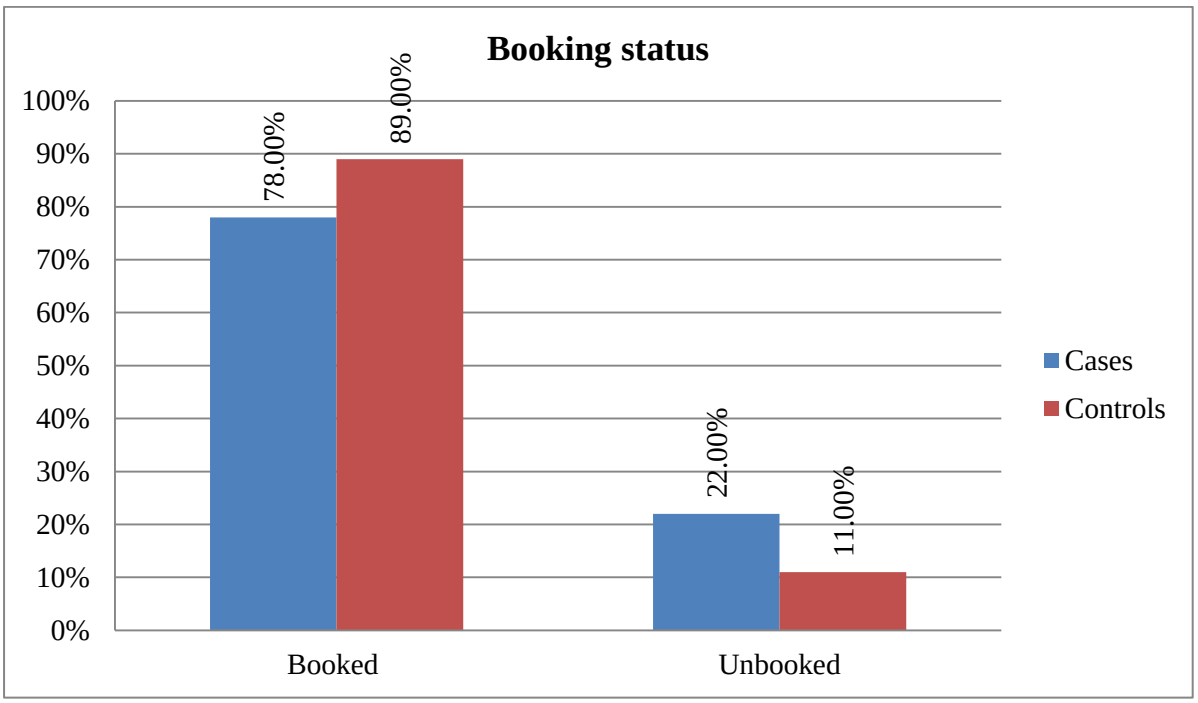

Table 3: Pre-pregnancy BMI among cases and controls. (n=100 in each group)

BMI	Group	
	Cases (%)	Controls (%)
<18	18(18)	15(15)
18 to 24.9	67(67)	72(72)
≥25 to 29.9	15(15)	13(13)

$\chi 2 = 0.595$, df = 2, p = 0.743

none of the patients in our study were obese; the BMI of all the cases and controls in this study fell below 30kg/m^2. Around 1/6th of our population were judged as underweight bases on their BMI which was <18kg/m^2. The majority of cases and controls had normal BMI. There was no statistical difference in pre-pregnancy BMI distribution between the two groups.

graph 3: Pre-pregnancy BMI among cases and controls.

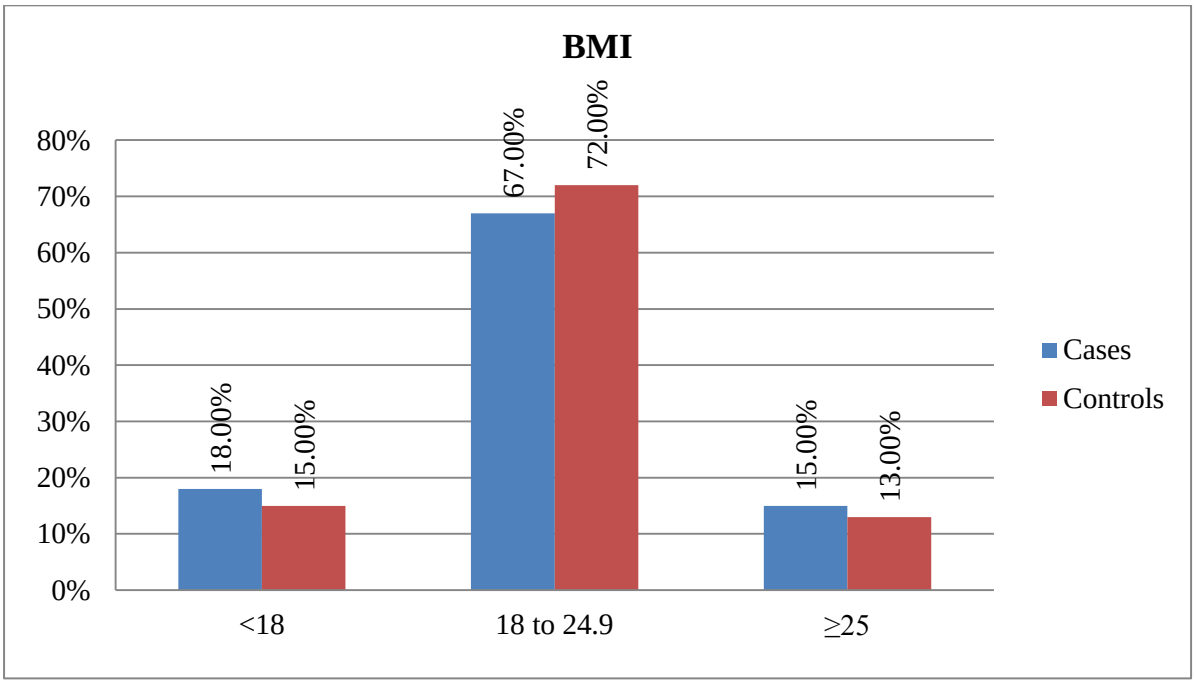

Table 4: Socioeconomic status among cases and controls (n=100 in each group)

Socioeconomic class	Group	
	Cases (%)	Controls (%)
1-upper class	2(2)	4(4)
2-upper middle class	12(12)	29(29)
3-middle class	61(61)	54(54)
4-lower middle class	18(18)	10(10)
5-lower class	7(7)	3(3)

$\chi 2 = 12.02$, df = 4, p = 0.017*

There was no significant difference in distribution among cases and controls when each socioeconomic class was taken into consideration. However, majority (86%) of the population among cases fell in socioeconomic class 3 or below whereas only 67% amongst controls was present in these classes. This difference was found to be statistically significant.

Graph 4: Socioeconomic status among cases and controls

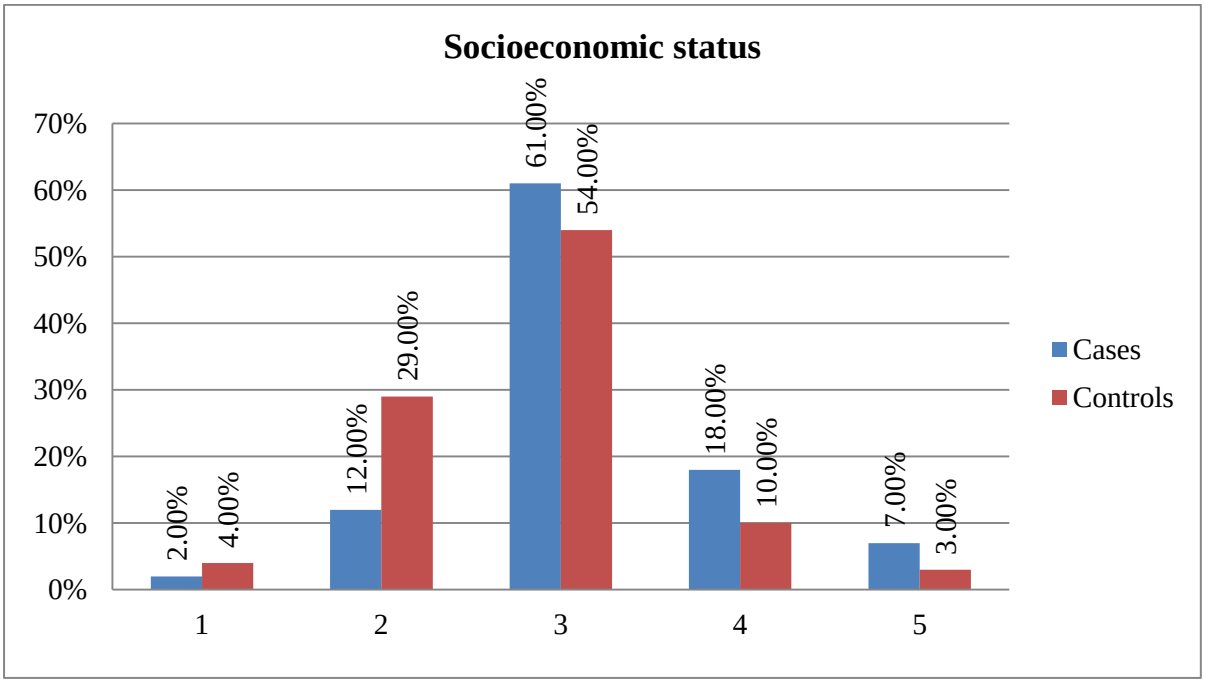

Table 5: Occupation among cases and controls (n=100 in each group)

occupation	Group			
	Cases (%)		Controls (%)	
Homemaker	76	76.0%	88	88.0%
Working women	24	24%	12	12%

$\chi 2 = 4.878$, $p = 0.0272$*

Among cases and controls majority i.e. 76% and 88% were homemakers respectively. Working women constituted the rest of the patients and all of them were daily wage labourers involved in strenuous physical activity. Statistically significant difference in the incidence of PROM was noted between the two groups. Thus, strenuous physical activity can be associated with occurrence of PROM.

graph 5: Occupation among cases and controls

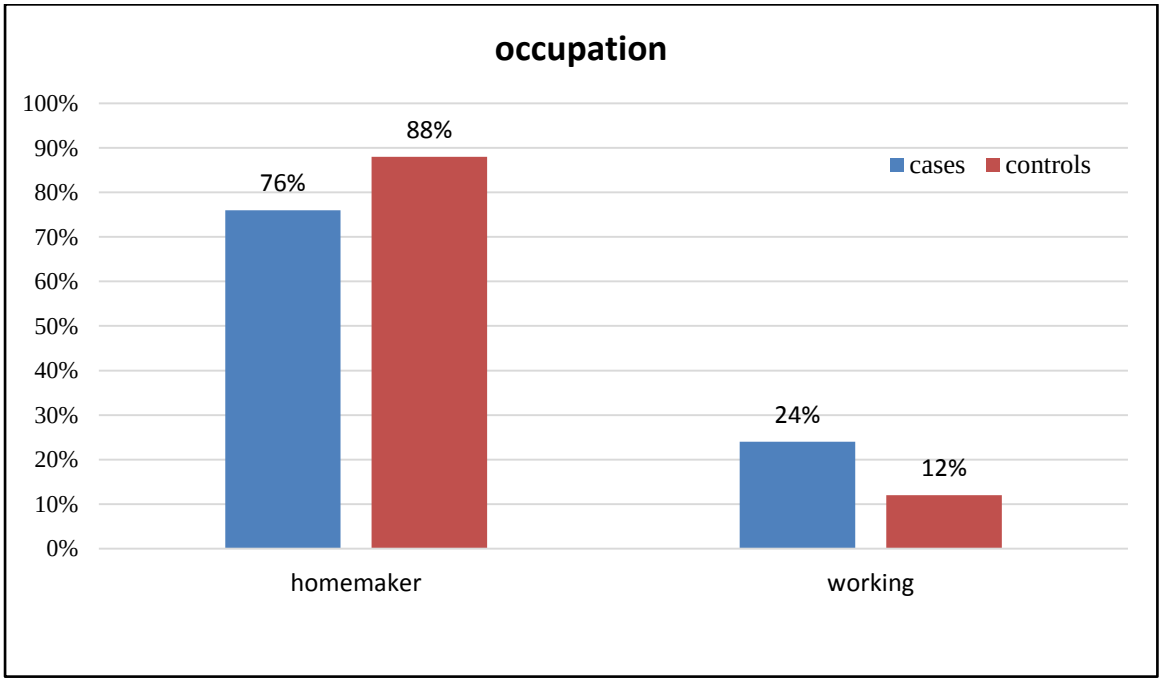

Table 6: obstetric index among cases and controls (n=100 in each group)

Obstetric index		Group	
		Cases (%)	Controls (%)
Primigravida		45(45)	35(35)
Multigravida	gravida 2	21(21)	31(31)
	gravida 3	15(15)	19(19)
	gravida 4	12(12)	10(10)
	gravida 5	6(6)	3(3)
	gravida 6	1(1)	2(2)

$\chi 2 = 5.159$, df = 5, p = 0.397

Among cases 45% were Primigravida and 55% were Multigravida and among controls 35% were Primigravida and 65% were Multigravida. There was no significant difference in obstetric index between two groups.

graph 6: obstetric index among cases and controls

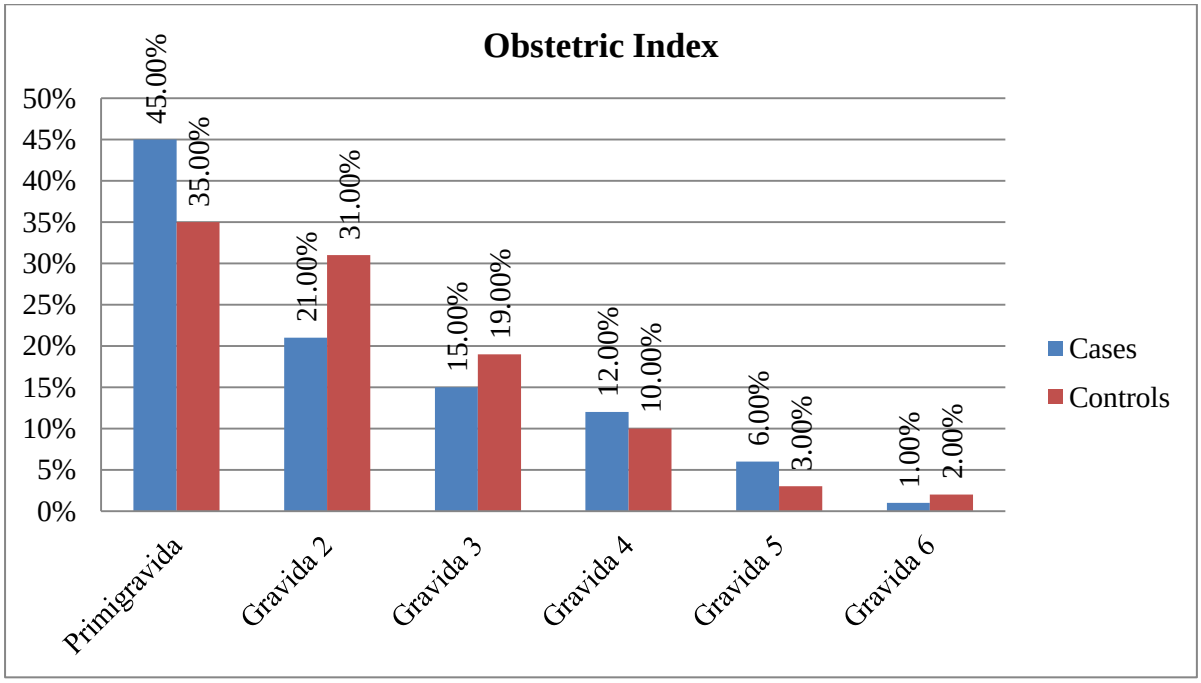

Table 7: Previous pregnancy risk factor comparison among Multigravida subjects

previous pregnancy risk factors	Group		P value
	Cases n=55	Controls n=65	
Abortion	5(9.1%)	1(1.5%)	0.059
Previous PROM	11(20%)	2(3.1%)	0.003*
H/o previous preterm delivery	7(12.7%)	2(3.1%)	0.046*

Among Cases 9.1% had previous history of abortion, 20% had previous PROM and 12.7% had h/o previous preterm delivery. Among controls 1.5% had previous history of abortion, 3.1% had previous PROM and 3.1% had H/o previous preterm. Significant difference was observed in History of Previous PROM and H/o previous preterm delivery between cases and controls.

graph 7: Previous pregnancy risk factor comparison among Multigravida subjects

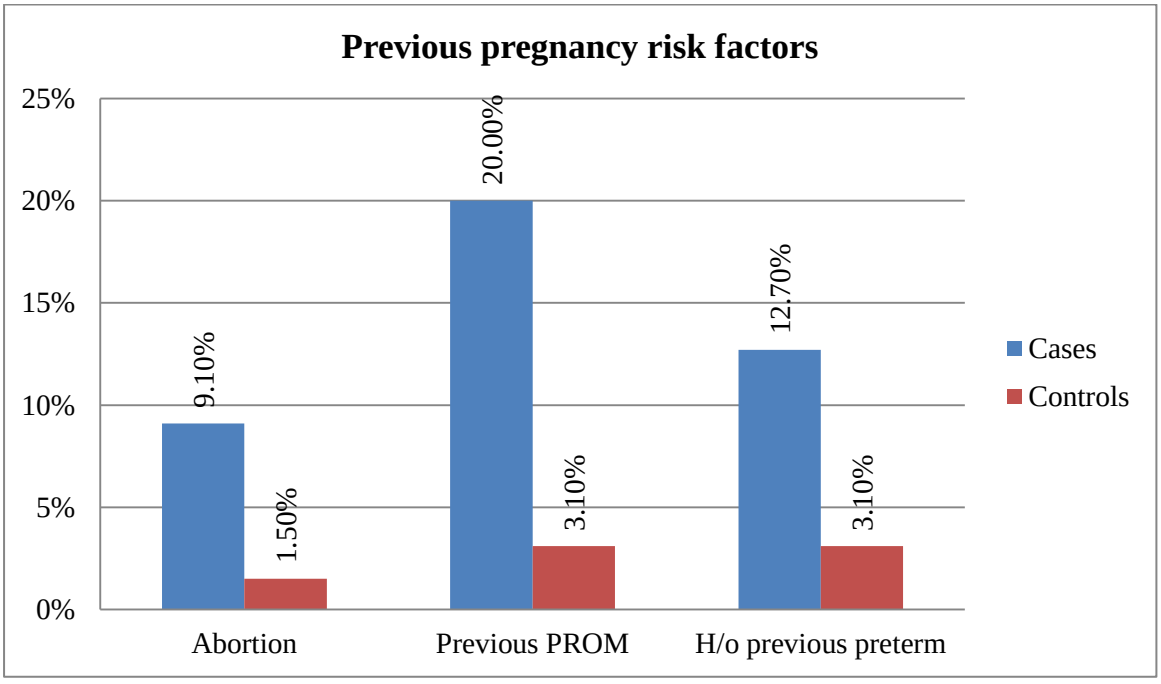

Table 8: Risk factors in present pregnancy among cases and controls (n=100 in each group)

	Group		P value
	Cases (%)	Controls (%)	
UTI	12(12)	4(4)	0.037*
White discharge p/v	13(13)	3(3)	0.009*
Malpresentation	9(9)	3(3)	0.074
H/o recent coitus	7(7)	4(4)	0.352
cervical encerclage	4(4)	3(3)	0.700
Early vaginal bleeding	7(7)	3(3)	0.194
Polyhydramnios	8(8)	2(2)	0.052
Anaemia	10(10)	2(2)	0.017*
GDM	2(2)	2(2)	1.000
Invasive procedures	4(4)	0(0)	
Tobacco chewing/smoking	4(4)	0(0)	

There was statistical difference between the incidence of the following risk factors such as occurrence of UTI, subjects with complaints of excess white discharge p/v, incidence of anaemia, h/o invasive procedures and tobacco chewing/smoking. Incidence of all the other risk factors was more in the PROM group when compared to controls but was not statistically significant.

Graph 8: Risk factors in present pregnancy among cases and controls

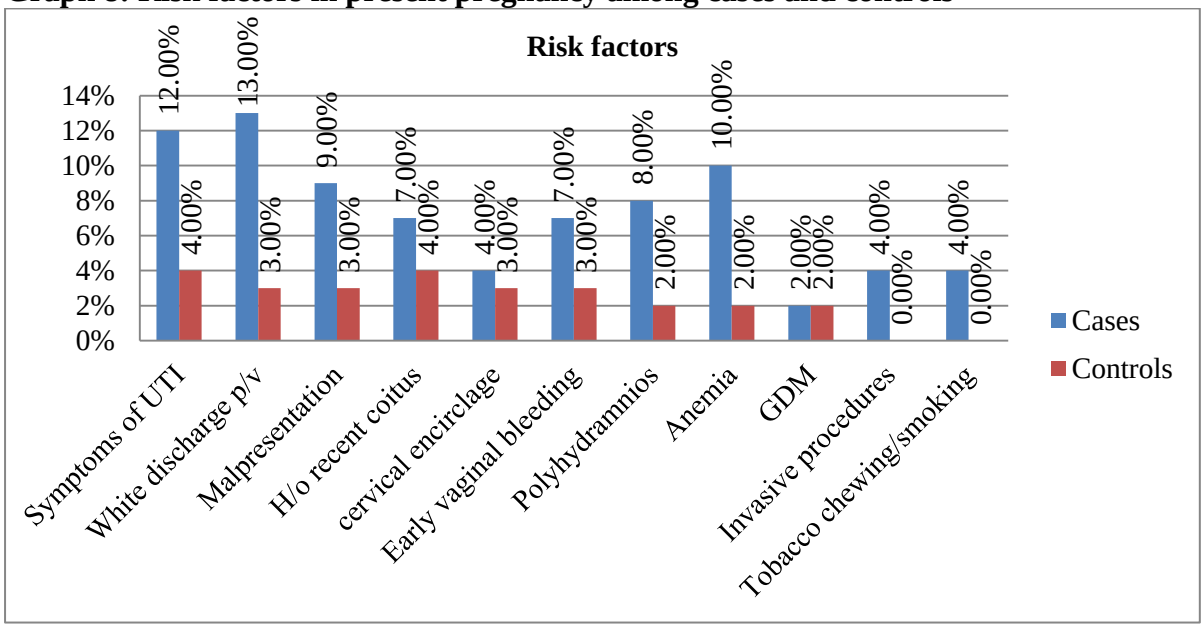

Table 9: Amniotic fluid index among cases and controls (n=100 in each group)

AFI	Group	
	Cases (%)	Controls (%)
≤5	24(24)	2(2)
>5	76(76)	98(98)

χ 2 = 21.39, df = 1, p <0.001*

Mean AFI of cases was 7.9 ± 5.0 and Mean AFI of controls was 11.44 ± 2.8. This difference in mean AFI between two groups was statistically significant.

graph 9: Amniotic fluid index among cases and controls

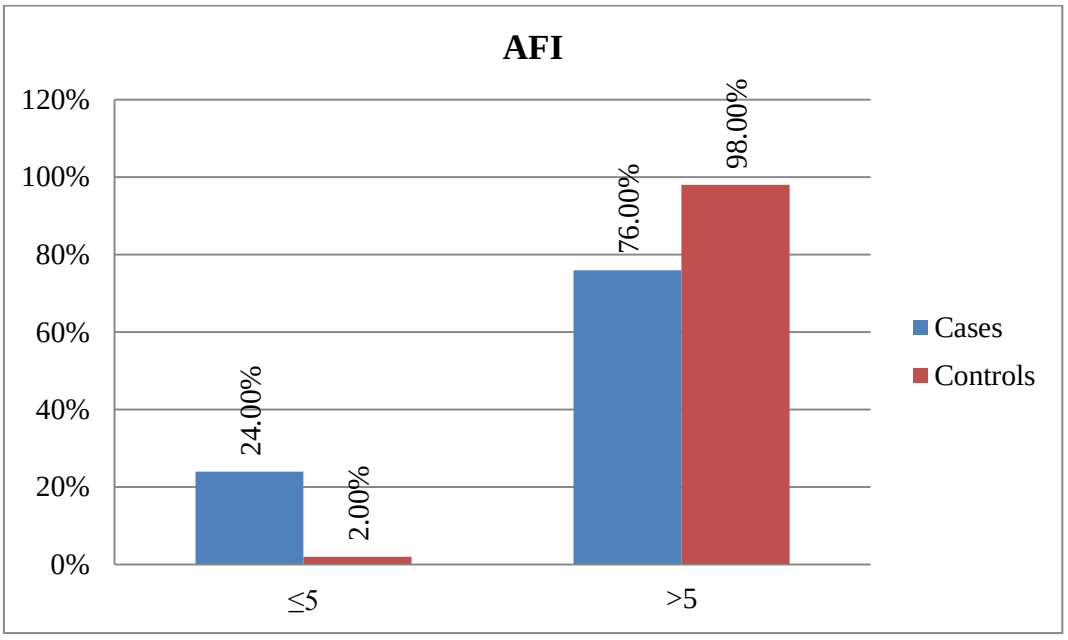

Table 10: White blood cell count among cases and controls (n=100 in each group)

WBC	Group	
	Cases (%)	Controls (%)
<17000	61(61)	88(88)
≥17000	39(39)	12(12)

$\chi 2 = 19.18$, df = 1, p <0.001*

graph 10: White blood cell count among cases and controls

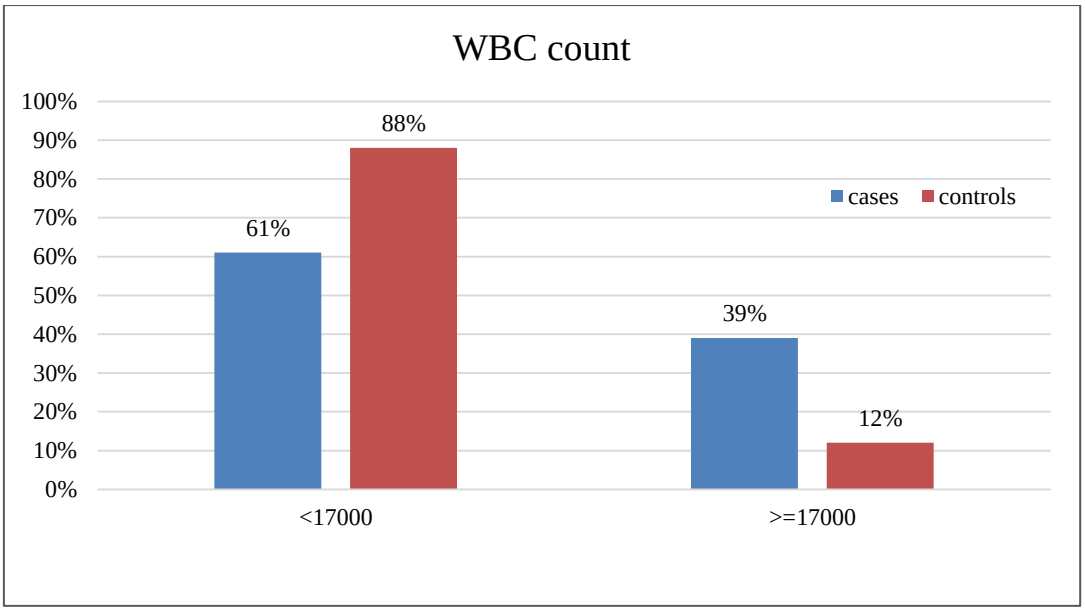

Table 11: C reactive protein (CRP) among cases and controls (n=100 in each group)

CRP	Group	
	Cases (%)	Controls (%)
Negative	75(75)	95(95)
Positive	25(25)	5(5%)

$\chi 2 = 15.68$, df = 1, p <0.001*

Among cases 25% were positive for CRP and among controls 5% were positive for CRP. This difference in CRP between two groups was statistically significant.

graph 11: C reactive protein (CRP) among cases and controls

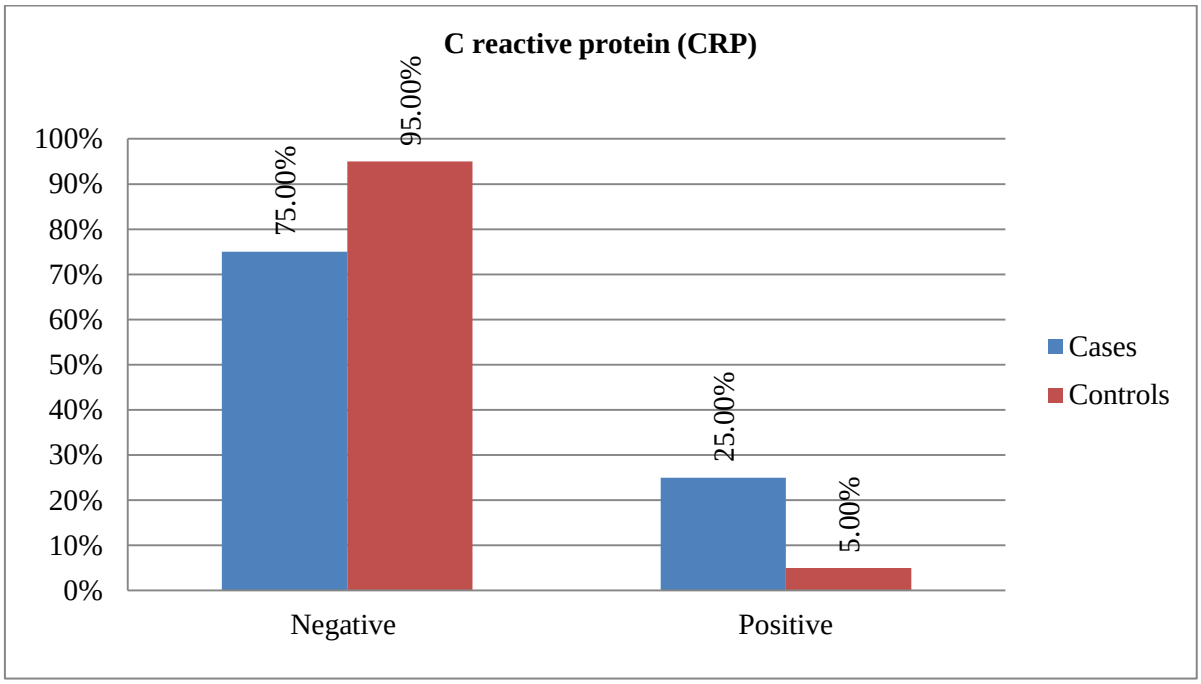

Table 12: Vaginal swab culture among cases and controls (n=100 in each group)

vaginal swab culture		Group	
		Cases (%)	Controls (%)
Normal vaginal flora		77(77)	94(94)
Infection	Fungal(Candida)	14(14)	6(6)
	Bacterial	9(9)	0(0)

$\chi 2 = 13.89$, df = 2, p = 0.001*

Among cases14 (14%) showed growth of the fungal pathogen, Candida and 9(9%) showed growth of bacterial pathogens accounting for an isolation rate of 23 (23%). In contrast, among controls only 6(6%) of the swabs yielded Candida and none yielded any bacterial pathogen. The difference in the isolation rate of the pathogens between the two groups was statistically significant (p=0.001).

The breakup of the pathogens in the PROM group was as follows: Candida species 14(14%), Escherichia coli 4(4%), Pseudomonas aeruginosa 3(3%), Enterobacter species 1(1%) and Streptococcus pyogenes 1(1%).

graph 12: Vaginal swab culture among cases and controls

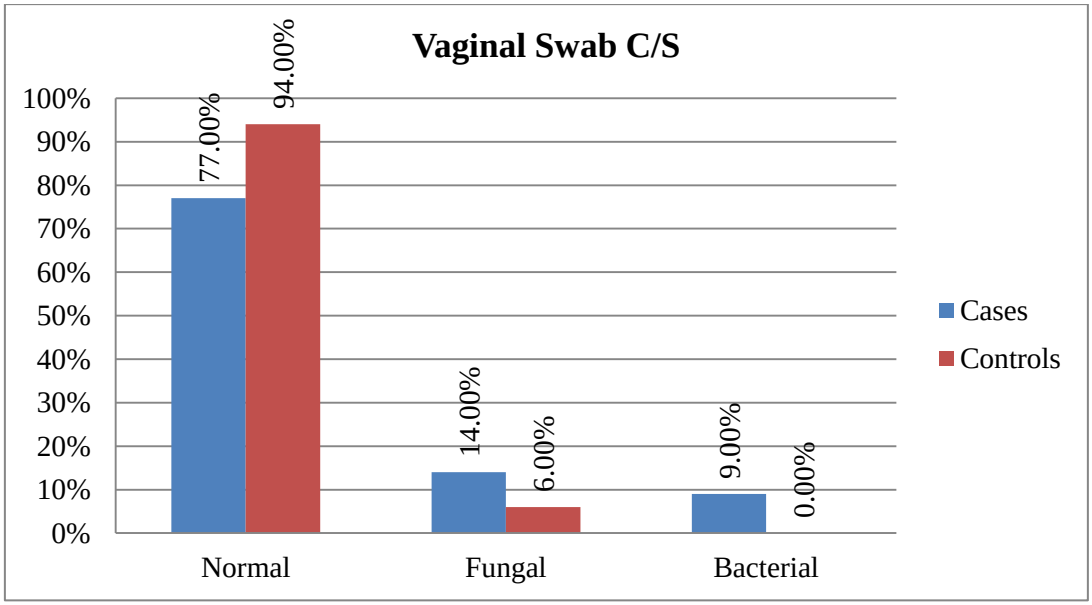

Table 13: sensitivity pattern of pathogenic bacteria (other than normal vaginal flora) cultured from high vaginal swabs

Antibiotic (disc strength)	Streptococcus pyogenes(n=1)	E. coli(n=4)	Enterobacter(n=1)	Pseudomonas(n=3)
Penicillin-G (10 units)	1(100)	2(50)	0(0)	-
Cefotaxime (30mcg)	-*	2(50)	0(0)	3(100)
Ceftazidime(30mcg)	-	2(50)	0(0)	3(100)
Ceftriaxone (30mcg)	-	2(50)	0(0)	3(100)
Cefipime (30mcg)	-	2(50)	0(0)	3(100)
Piperacillin (100mcg)	-	2(50)	0(0)	3(100)
Ciprofloxacin (5mcg)	-	4(100)	1(100)	3(100)
Levofloxacin (5mcg)	0(0)	4(100)	1(100)	3(100)
Amikacin (30mcg)	-	4(100)	1(100)	3(100)
Gentamycin (10mcg)	-	4(100)	1(100)	3(100)
Tobramycin (10mcg)	-	4(100)	1(100)	3(100)
Tetracycline (30mcg)	-	2(50)	1(100)	3(100)
Trimethoprim/Sulfamethoxazole (1.25/23.75mcg)	-	2(50)	1(100)	3(100)
Chloramphenicol (30mcg)	1(100)	-	-	-
Erythromycin (15mcg)	1(100)	-	-	-
Clindamycin (2mcg)	1(100)	-	-	-

*if Streptococcus pyogenus is sensitive to Penicillin it is not tested for sensitivity to other higher cell wall acting antibiotics as it is known to be obviously sensitive to them also.

Antibiotic sensitivity testing from our study showed that 50% of E coli were Extended spectrum beta lactamase(ESBL) producers resistant to cell wall acting antibiotics such as

cephalosporins. They were also resistant to Piperacillin, Tetracycline and Trimethoprim/Sulfamethoxazole, but sensitive to Aminoglycosides: Amikacin, Gentamycin, Tobramycin and to gyrase inhibitors: Ciprofloxacin, Levofloxacin.

Only one swab culture showed growth of Enterobacter species which was also found to be an ESBL producer resistant to Cephalosporins and Piperacillin but sensitive to Aminoglycosides, Tetracyclines, Trimethoprim/Sulfamethoxazole and Quinolones.

A total of 3(3%) cases of Pseudomonas aeruginosa were identified which were sensitive strains exhibiting sensitivity to Cephalosporins, Piperacillin, Quinolones and Aminoglycosides. The lone Streptococcus Pyogenes isolated was a Penicillin sensitive strain. Thus 66.6% of the pathogens were found to be sensitive to Cephalosporins.

Table 14: Analysis of PROM according to laboratory investigations for evidence of infection (n=100 for both groups)

Investigations	Group		P value
	Cases (%)	Controls (%)	
Positive CRP	25(25)	5(5)	<0.001*
Positive vaginal swab culture	23(23)	6(6)	<0.001*
WBC>17000	39(39)	12(12)	<0.001*
Abnormal Urine microscopy	16(16)	5(5)	0.011*

All the laboratory indicators for infection showed statistical significance in cases when compared with controls.

graph 13: Analysis of PROM according to laboratory investigations for evidence of infection

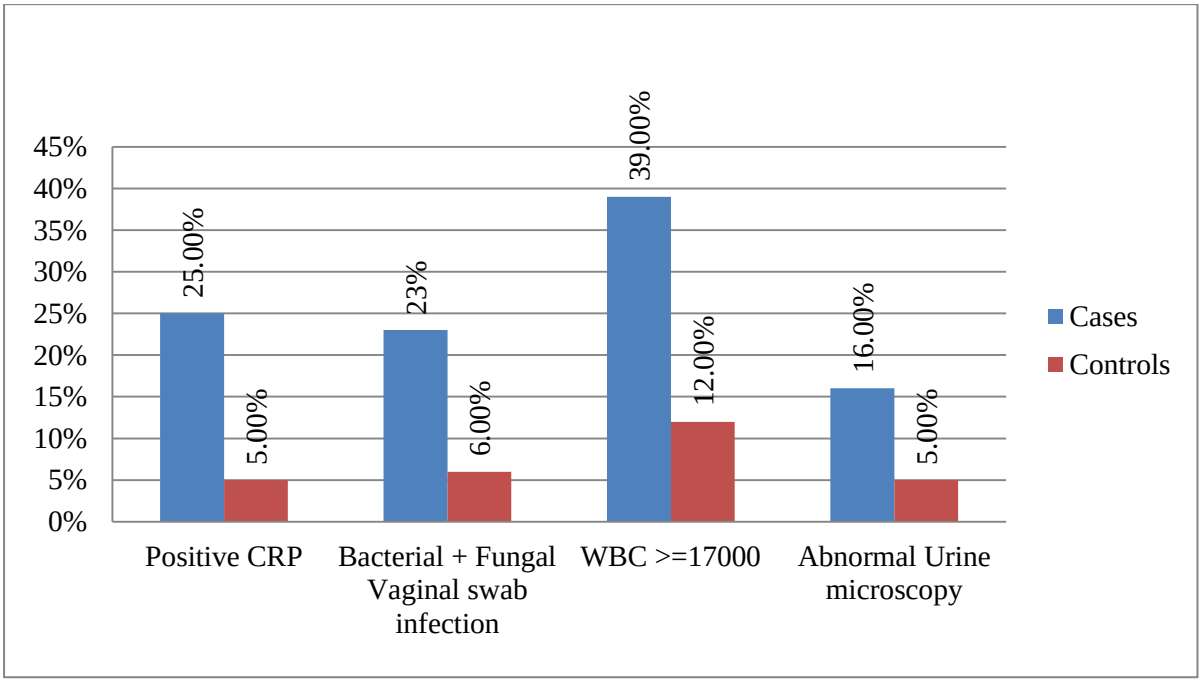

Table 15: Mode of delivery among cases and controls (n=100 in each group)

mode of delivery	Group	
	Cases (%)	Controls (%)
Vaginal Delivery	50(50)	67(67)
Caesarean Section	50(50)	33(33)

$\chi 2 = 5.95$, df = 1, p = 0.015*

Caesarean section was performed in 50% of cases and 33% among controls. A significant number of cases required caesarean section when compared with controls.

graph 14: Mode of delivery among cases and controls

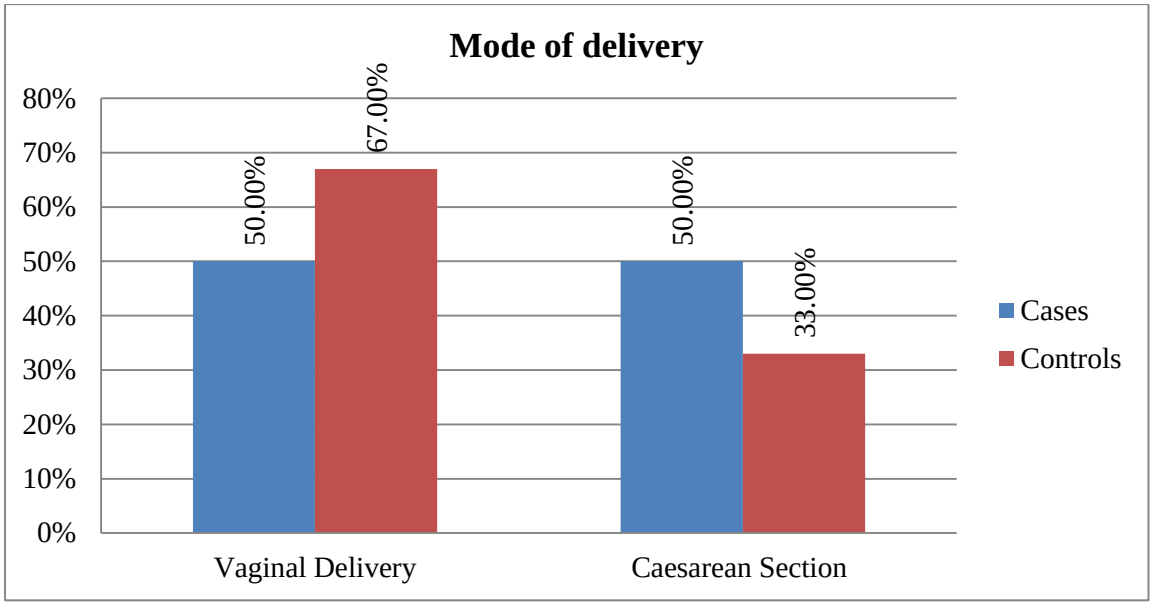

Table 16: Indications for Caesarean Section among cases and controls

Indication	Caesarean section		P value
	Cases(n=50)	Controls(n=33)	
Fetal distress	23(46%)	3(9.1%)	<0.001*
Oligohydramnios	13(26%)	1(3%)	0.006*
Failed induction	13(26%)	3(9.1%)	0.056
Previous LSCS	7(14%)	10(30.3%)	0.072
Cord prolapse	2(4%)	0(0%)	
CPD	3(6%)	2(6.1%)	0.991
Malpresentation	5(10%)	4(12.1%)	0.761
Maternal desire	3(6%)	5(15.2%)	0.167
Other indications	4(8%)	6(18.2%)	0.163

Most common indication for LSCS among cases was fetal distress (46%) and among controls was previous LSCS (30.3%). Indications such as fetal distress and oligohydramnios were significantly more among the cases.

graph 15: Indications for Caesarean Section among cases and controls

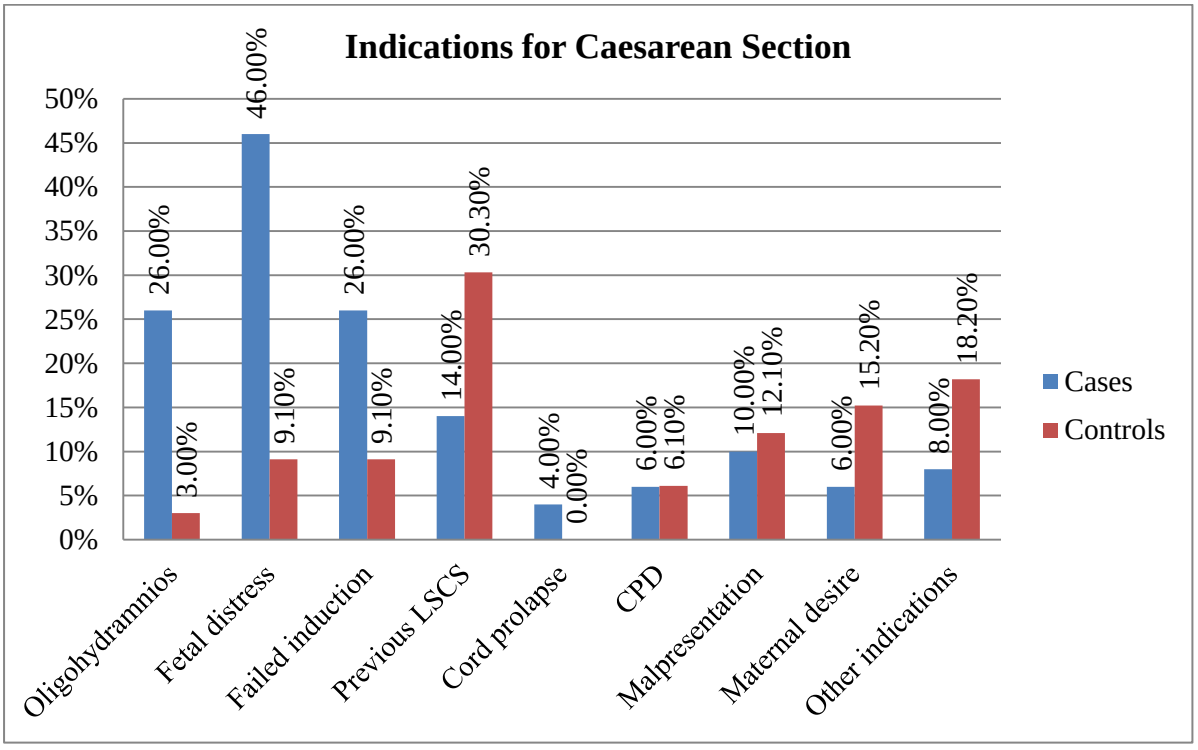

Table 17: Maternal complications among cases and controls (n=100 in each group)

Maternal complications	Group		P value
	Cases (%)	Controls (%)	
Clinical chorioamnionitis	8(8)	0(0)	
PPH	6(6)	3(3)	0.306
Abruption	4(4)	3(3)	0.700
Puerperal pyrexia	12(12)	2(2)	0.006*
Retained placenta	6(6)	1(1)	0.054
Foul smelling lochia	5(5)	0(0)	
Wound infection	9(9)	2(2)	0.030*
Hospital stay >10 days	12(12)	0(0)	

Among cases 8% had clinical chorioamnionitis antenatally 6% had PPH, 4% had Abruption, 12% had Puerperal pyrexia, 6% had Retained placenta, 5% had foul smelling lochia and 9% had Wound infection. A significant percentage of women had to stay in the hospital for >10days. In controls 3% had PPH and abruption respectively, 2% had Puerperal pyrexia and wound infection respectively, 1% had retained placenta and no patients had prolonged hospital stay. Significant difference in maternal complications was observed for Clinical chorioamnionitis, Puerperal pyrexia, Foul smelling Lochia, Wound infection and prolonged hospital stay between the two groups.

graph 16: Maternal complications among cases and controls

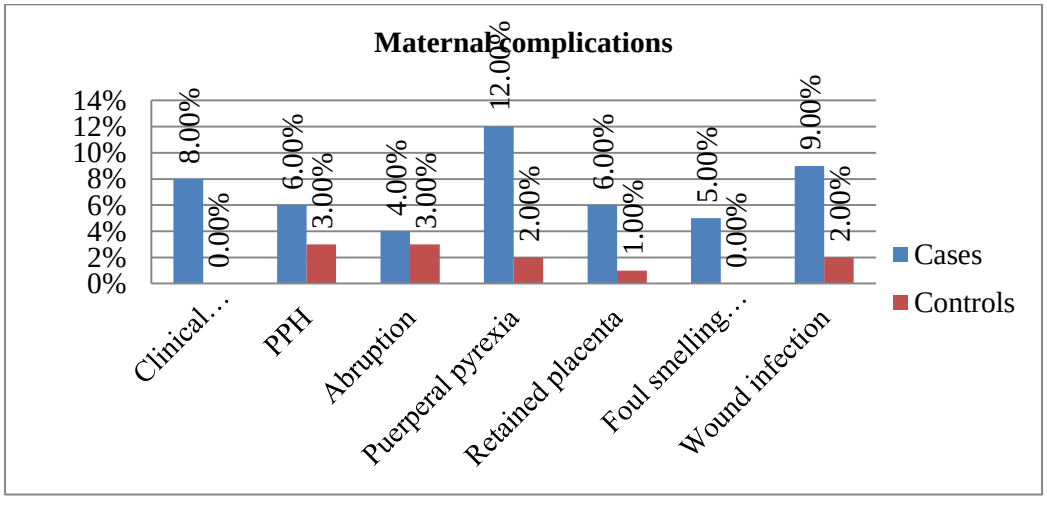

Table 18: Birth weight of babies among cases and controls (n=100 in each group)

Birth weight(Kg)	Group	
	Cases (%)	Controls (%)
<1.5	10(10)	2(2)
1.5 to 2.5	46(46)	32(32)
>2.5to 3	25(25)	27(27)
>3	19(19)	39(39)

$\chi 2 = 14.82$, df = 3, p = 0.002*

In Cases 56% had Low birth weight (<2.5kgs) and in controls 34% had Low birth weight (<2.5kgs). This difference in low birth weight between two groups between two groups was statistically significant.

graph 17: Birth weight of babies among cases and controls

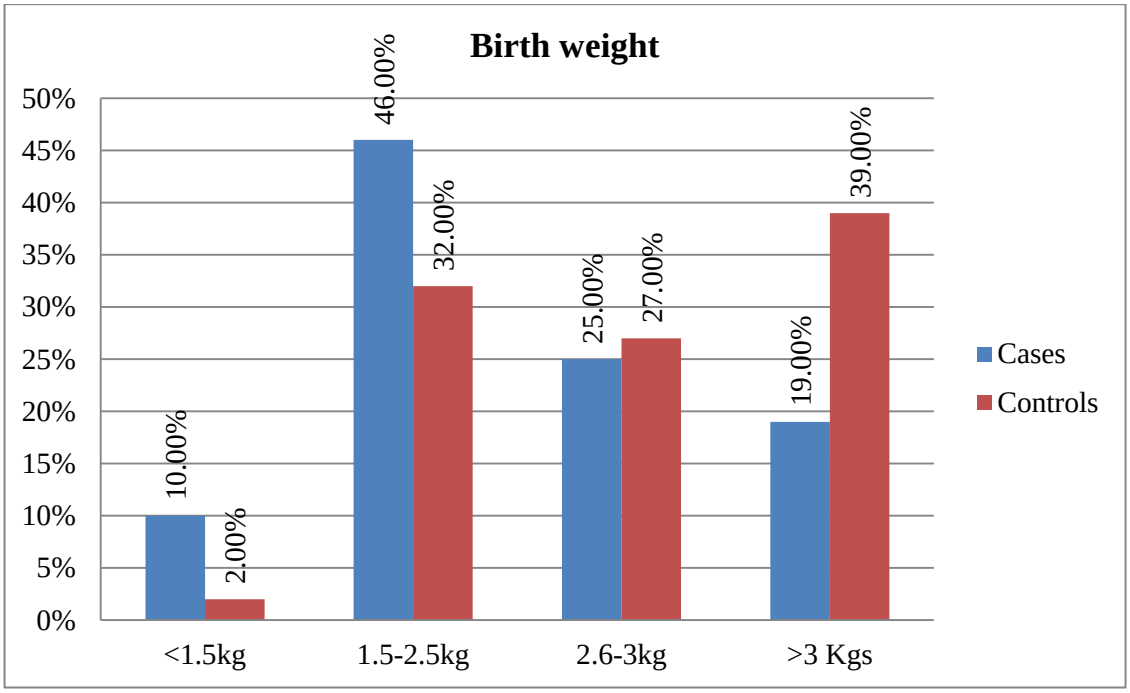

Table 19: APGAR score among cases and controls (n=100 in each group)

APGAR at 5 minutes	Group	
	Cases (%)	Controls (%)
>5	73(73)	96(96)
≤5	27(27)	4(4)

$\chi 2 = 20.195$, df = 1, p <0.001*

Low Apgar was more commonly seen among cases (27%) when compared to controls(4%)This difference in Apgar score at 5 min was statistically significant.

graph 18: APGAR score among cases and controls

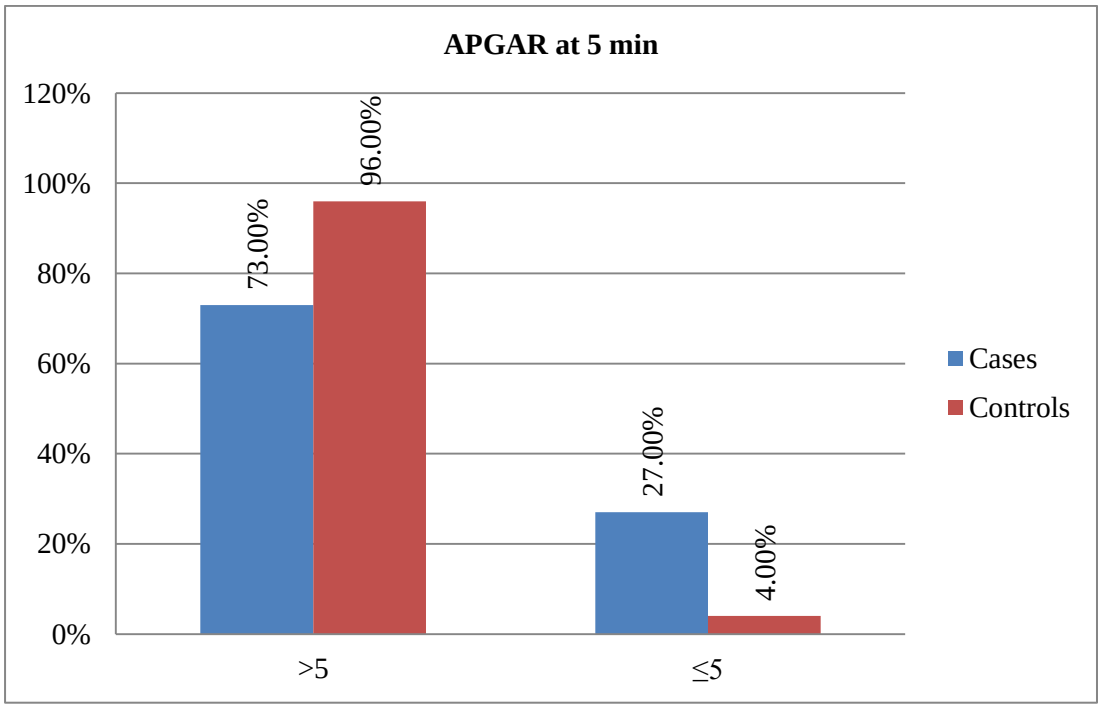

Table 20: Still birth among cases and controls (n=100 in each group)

	Group	
	Cases (%)	Controls (%)
Live birth	96(96)	99(99)
Still birth	4(4)	1(1)

$\chi 2 = 1.846$, df = 1, p = 0.174

Among Cases 4% had still birth and in controls 1% had still birth. There was no significant difference in Still birth between two groups.

Table 21: NICU admission among cases and controls (n=100 in each group)

NICU admission	Group	
	Cases (%)	Controls (%)
No	58(58)	95(95)
Yes	38(38)	4(4)

$\chi 2 = 36.43$, df = 1, p <0.001*

Among cases 39.6% of neonates required NICU admission and among controls 4% required NICU admission. This difference in NICU admission between two groups was statistically significant.

graph 19: NICU admission among cases and controls

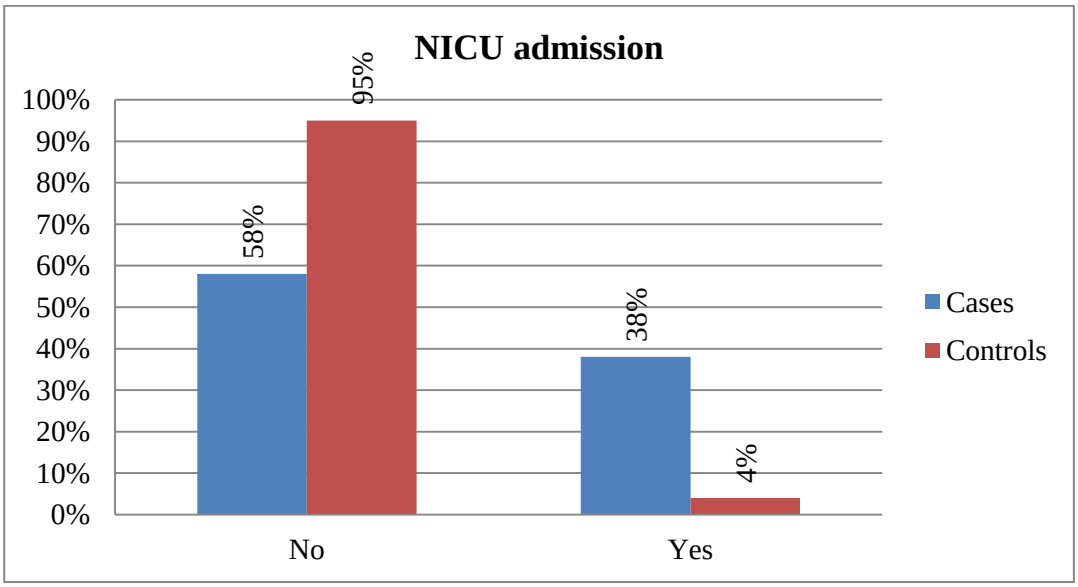

Table 22: Duration of NICU stay among cases and controls

Duration of NICU stay	Group	
	Cases (n=38)	Controls (n=4)
<7 days	37(37%)	4(4%)
7 to 14 days	1(1%)	0(0%)

χ 2 = 0.108, df = 1, p = 0.743

Thirty eight percent neonates among cases and 4% of controls required NICU admission. Among cases, duration of NICU stay was <7 days in 97.4% and in 2.6% duration was 7 to 14 days. Among the controls for all 4 babies admitted to NICU duration of stay was <7 days. There was no significant difference in duration of NICU stay between two groups.

graph 20: Duration of NICU stay among cases and controls

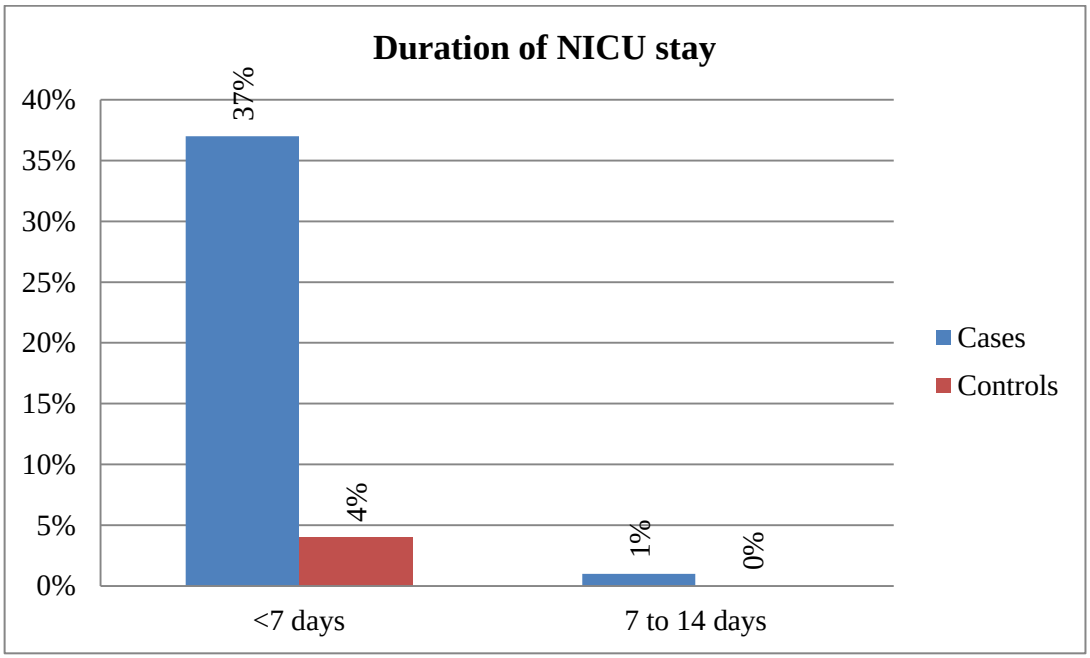

Table 23: Neonatal Complications among cases and controls (n=100 in each group)

Neonatal complication	Group		P value
	Cases (%)	Controls (%)	
Birth asphyxia	13(13)	2(2)	0.003*
Jaundice	13(13)	3(3)	0.007*
Neonatal sepsis	13(13)	0(0)	
Intraventricular hemorrhage	5(5)	0(0)	
Neonatal death	5(5)	0(0)	

Among cases 13% had Birth asphyxia, Jaundice and Neonatal sepsis respectively and 5% had Intraventricular hemorrhage and neonatal death. Among controls 2% had Birth asphyxia and 3% had Jaundice. There was significant difference in complications such as birth asphyxia and jaundice between cases and controls. Neonatal sepsis, intraventricular hemorrhage and neonatal death did not occur in the control group.

graph 21: Neonatal Complications among cases and controls

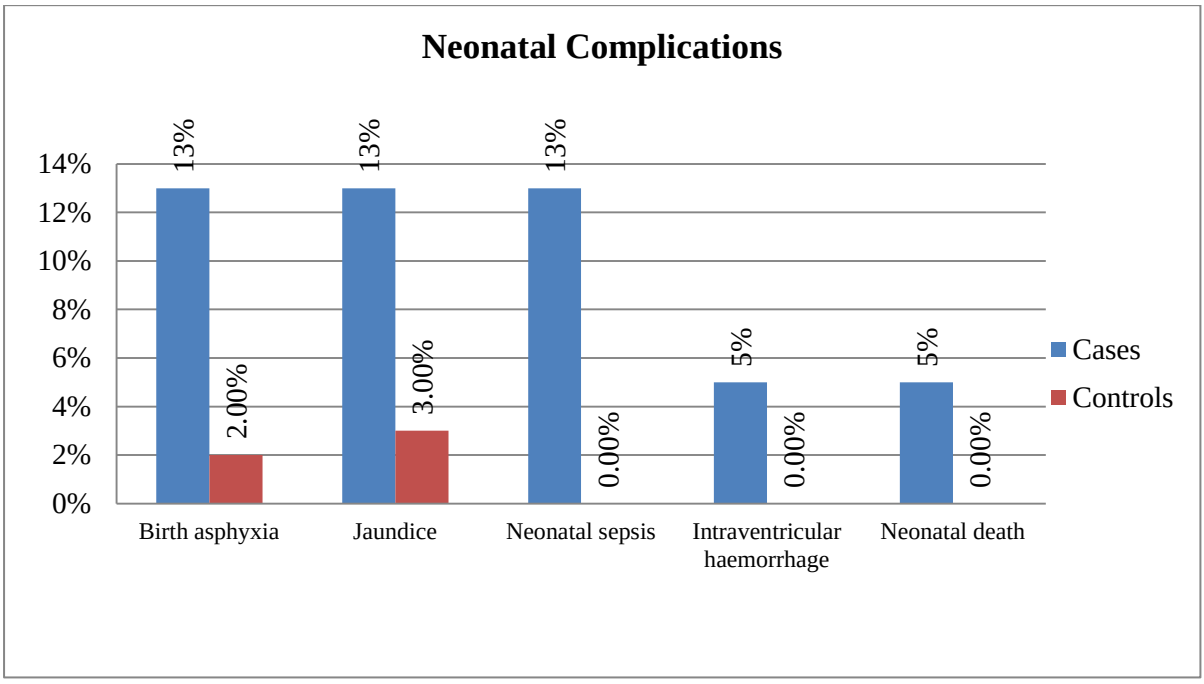

Table 24: duration between PROM to delivery among cases(n=100)

PROM- delivery interval in hours	number (%)
0-24	61 (61)
25-48	23 (23)
>48	16 (16)

Table 25: Neonatal morbidity and mortality in relation to duration between PROM to delivery among cases

Neonatal complication	PROM-delivery interval		P value
	≤24hrs (n=61)	>24hrs (n=39)	
Still Birth	1 (1.6%)	3 (7.7%)	0.132*
Birth Asphyxia	6 (9.8%)	7 (17.9%)	0.138
Jaundice	10 (16.4%)	3 (7.7%)	0.167
Neonatal Sepsis	2 (3.3%)	11 (28.2%)	<0.001*
Intraventricular Hemorrhage	1 (1.6%)	4 (10.3%)	0.043*
Neonatal Death	3 (4.9%)	2 (5.1%)	0.319

Percentage of stillbirths, birth asphyxia, neonatal sepsis, intraventricular hemorrhage and neonatal death increased with increase in PROM- delivery interval. Significant difference in rate of stillbirth, neonatal sepsis and intraventricular hemorrhage was observed for patients with PROM- delivery interval >24 hours.

graph 22: Neonatal morbidity and mortality in relation to duration between PROM to delivery among cases

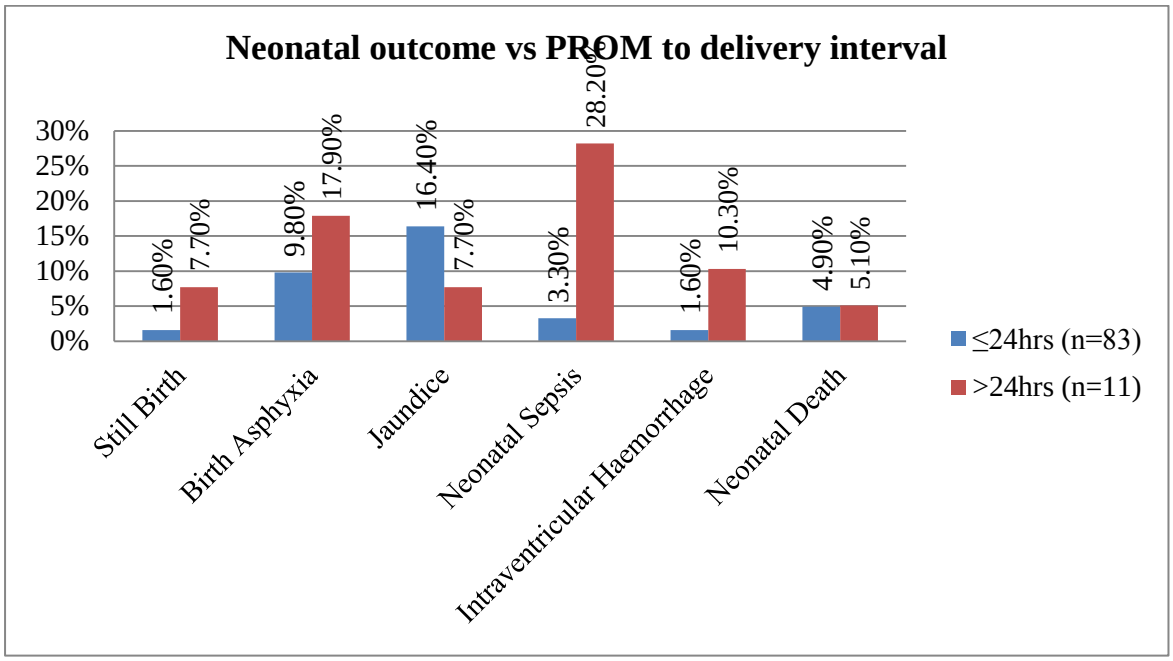

Table26-Neonatal morbidity in relation to gestational age among cases

	28-33 weeks	**34-36weeks**	**≥37weeks**
No of babies	17	26	57
Mean birth weight (Mean ± SD)	1.6	2.3	2.7
No of babies with birth wt≤2.5kg	17(100%)	18(69.2%)	21(36.8%)
Mean PROM-delivery interval in hours	50.7	24.2	23.1
No of NICU admissions	16(94.1%)	14(53.8%)	8(14%)
Stillbirths	1(5.9%)	2(7.7%)	1(1.8%)
Neonatal death	3(17.6%)	2(7.7%)	0

Out of the total 100 cases, 57 were term PROM (≥37weeks gestation). 36.8% of the term babies had birth weight ≤2.5kg. PROM- delivery interval decreased as period of gestation increased. Stillbirths and neonatal deaths were less in the babies born at term gestation.

Table 27Association between Perinatal outcome & Oligohydramnios comparison between two groups

	Group					
	Cases			Controls		
	AFI			AFI		
	≤5 (n=24)	>5	P value	≤5 (n=2)	>5	P value
Perinatal mortality	37.5%	0.0%	<0.001*	0.0%	1.0%	0.886
APGAR at 5min ≤5	54.2%	18.4%	0.001*	0.0%	4.1%	0.771
NICU admission	45.8%	35.5%	<0.001*	0.0%	4.1%	0.948
LSCS	62.5%	46.1%	0.160	100.0%	31.6%	0.042*

In cases among those with AFI ≤5, 37.5% had Perinatal mortality,54.2% had ≤5 APGAR at 5 minutes, 45.8% had NICU admission and 62.5% had LSCS and among those with AFI >5, 0% had Perinatal mortality, 18.4% had ≤5 APGAR at 5min, 35.5% NICU admission and 46.1% had LSCS. The difference in perinatal mortality, APGAR at 5min and NICU admission between two groups of AFI was statistically significant. Among controls significant difference was observed for LSCS between AFI ≤5 and >5.

DISCUSSION

Analysis of PROM according to maternal age. (table 1)

In our study majority of subjects in both the groups were in the age group 20 to 25 years. The mean age in PROM patients in the study was 25.5 years. There was no significant difference in age distribution between two groups. Thus, age may not be a significant risk factor in PROM.

In a study by Rajarathnam et al[77] in Mangalore, Karnataka (2014), majority belonged to the age group of 18-30years.

In a study done by Ibishi et al[78] in Japan, majority of the study participants were between 20-29 years.

Shweta et al[79] and Okeke et al[80] also reported majority of patients to be in the 20-29 years age group (79% and 58.2% respectively).

All the above studies are comparable with the present study.

MEAN AGE IN PATIENTS WITH PROM

STUDY	MEAN AGE (IN YEARS)
Didem Akyol et al (1991)[81]	24.6
Pajntar M et al (1997)[82]	25.73
Yossef Ezra et al (2004)[8]	28.6
Farhat Karim et al (2006)[83]	27
Ben Chong et al (2009)[84]	30.8
Naagar (2015)[85]	27.28
Musaba (2017)[86]	25
Present study	25.5

Analysis according to antenatal care(table2)

Analysis from the present study showed that 22% of the cases and only 11% among the controls were unbooked patients. In unbooked cases there is lack of antenatal care leading to lack of identification of recurrent risk factors like preterm delivery, induced abortions and PPROM. Also, urogenital infections are not detected and treated due to lack of antenatal care leading to PPROM. Our study shows a statistically significant difference in the booking status between cases and controls (78% Vs 89%, p=0.036).

However, this is in contrast with a study by Shwetha[76] which shows a high proportion of unbooked women (84%) among the PROM group.
In the study by Anjana Devi[87], 48% were unbooked in the PROM group compared to 37% in the control group.

About 23% of the study cases were unbooked as compared to 17% of the controls in a study by karat et al which is similar to our study. Rates of PROM positively correlated with women residing in rural areas, unbooked status and hailing from a lower socioeconomic background.[12]

Study	**Unbooked patients among PROM group**
Anjana Devi[87]	48%
Karat[12]	23%
Shweta Ananth[79]	84%
Shweta Patil[88]	31%
Bhupesh H Gaikwad[89]	76%
Present study	22%

The studies by Shweta Ananth and Bhupesh et al showed a higher incidence of unbooked cases among the PROM group whereas results from karat et al and Swetha Patil's studies were similar to our numbers.

Analysis of PROM according to body mass index(table3), socioeconomic status(table4) and occupation(table5)

socioeconomic status

In our study, majority (86%) of the population among cases fell in socioeconomic class 3 or below whereas only 67% amongst controls was present in these classes. This difference was found to be statistically significant(p=0.017). This suggests that lower socioeconomic status is associated with premature rupture of membranes. Modified B.G Prasad's socioeconomic scale was used to categorize the patients.[90]

However, it is not clear how socioeconomic status predisposes women to PPROM. It could be lack of access to health care, poor personal hygiene, physical activity or other factors associated with lower socioeconomic status like stress, depression, poor general health, or nutritional deficiencies associated with unhealthy lifestyles.

Studies have shown that malnourished women have a decreased level of host defence factors regularly present in amniotic fluid so infectious agents such as Escherichia coli and Staphylococcus aureus play a larger role.

In a study conducted in Mumbai in 2015 by Swetha et al[79], the incidence of patients hailing from lower socioeconomic status was 58% and middle socioeconomic status was 30% in contrast to our study which showed 61% among the middle and 25% among the lower socioeconomic status groups.

Swathi Pandey et al[52] reported low and middle socioeconomic status to be 61% and 39% respectively. In A study conducted in 2015 a majority of the study population (73%) were in the socioeconomic middle class.

Dars et al[91] in a study conducted in pakistan in 2014 reports that 72% PROM patients belonged to poor class, 21% to middle class and upper class accounted for 7%.

However, it is imperative to point that the incidence of PROM is significantly lower in women hailing from high socioeconomic groups implying the status of nutrition and access to health care plays a significant role

BMI

There was no significant difference in pre-pregnancy BMI distribution between the cases and controls in our study.

Occupation

In our study 24% of cases and 12% of controls belonged to working group and the remaining constituted homemakers. Working women were significantly at more risk for PROM compared to homemakers. In our study majority of the case population belonged to the socioeconomic class 3 or less who are more often employed as daily wage workers involved in strenuous physical activity which during pregnancy would have increased the risk of PROM.

Poverty, lack of education, poor nutrition, occupation, employment and residential stability are all interrelated socio demographic indicators. low socioeconomic status with associated factors like malnutrition, over exertion, poor hygiene, stress, high parity, recurrent genitourinary infections and anaemia considerably increase the risk of PROM.[92]

Analysis according to obstetric index (table 6)

In this study among cases 45% were Primigravida and 55% were Multigravida and among controls 35% were Primigravida and 65% were Multigravida which is comparable to the study by Swathi Pandey[52] (primigravida 52% and multigravida 48% among cases).

There was no significant difference in obstetric index between the two groups in our study.

Percentage of primigravidae in various studies

Study	Percentage
Yossef Ezra et al 2004[8]	58.3%
Didem Akyol et al 1991[81]	59.2%
Pajntar M et al 1997[82]	56.7%
Ben Chong et al 2009[84]	77.8%
Swathi Pandey et al 2000[52]	52%
Haiyan Yu et al 2015[93]	70.8%
Rajarathnam et al 2014[77]	83.6%
Endale et al 2016[94]	69.7%
Bhupesh H Gaikwad2016[89]	63%
Present study	45%

In our study, when cases and controls were compared there was no statistically significant difference in terms of obstetric index. However, if only PROM cases are taken into consideration, our study reflected a relatively higher incidence among multigravidas. With this in mind, other studies had a contrastingly higher incidence among primigravidae. It is important to point out that some of these other studies did not have a case control pattern rendering the impression that primigravidae are more susceptible to PROM, a moot point. Here in our study, the design being case control clearly delineates the fact that the obstetric index is not a parameter significant enough to be attributed to PROM.

Analysis according to past obstetric history in multiparous women(table7)

Clinically significant past obstetric history such as previous h/o abortions, PROM and preterm delivery were taken as parameters, out of which two parameters namely previous h/o PROM and preterm delivery turned out to be statistically significant.

Among the 55 multiparous patients in the PROM group, 11(20%), 7(12.7%) and 5(9.1%) experienced previous PROM, preterm delivery and abortions respectively. Among the controls there were a total of 65 multiparous women out of whom only 2(3.1%), 2(3.1%), and 1(1.5%) gave a history of previous PROM, preterm labour and abortions respectively. Significant difference was observed in History of Previous PROM and H/o previous preterm birth between cases and controls.

Prior spontaneous preterm delivery caused by PPROM and preterm delivery may be significantly associated with similar outcomes in the current gestation. (Mercer Bm and Goldenberg RL[95])

Our study is comparable with the study by Swathi Pandey in which the recurrence of PROM was 21% and 23% in a study by Fathima.

A study by Harger et al[96] reported after a multivariate logistic regression analysis that previous preterm delivery was an independent risk factor for PPROM with an odds ratio of 2.5 compared to controls.

Berkovitz et al[97] also identified previous preterm delivery as a risk factor for PPROM in the index pregnancy, reporting adjusted odds ratio of 3.2 for PPROM.

Experiencing PROM in the first pregnancy may cause the woman to undergo biological changes that predispose her to experiencing PROM in subsequent pregnancies, or there may be other environmental or biologic factors that predispose a woman to PROM.

Risk factors from previous pregnancy in various studies:

Maternal risk factor	Vlora Ademi Ibishi 2015[78]	Singh Uma et al 2007[98]	Pandey Kiran[99] et al 2010	Present study
Previous PROM	59%	25.9%	30%	20%
Previous preterm birth	-	18.15%	14.14%	12.7%
Previous abortion	29%	25.2%	14.14%	9.1%

All the above, mentioned studies show a risk of PROM recurrence in subsequent pregnancy. Hence there is a need for early detection of risk factors and appropriate treatment.

Analysis according to risk factors in the present pregnancy(table8)

In this study the risk factors for PROM in the present pregnancy were urogenital infections 25%(symptoms of urinary tract infection 12%, abnormal per vaginal discharge 13%) anaemia 10%, malpresentations 9%, polyhydramnios 8%, recent coitus 7%, early vaginal bleeding 7%, cervical encerclage 4%, invasive procedures 4%, tobacco chewing/smoking 4%.

There was statistical difference between the incidence of the following risk factors such as symptoms of urinary tract infection, subjects with complaints of excess white discharge per vagina, incidence of anaemia, h/o invasive procedures and tobacco chewing/smoking. Incidence of all the other risk factors was more in the PROM group when compared to controls but was not statistically significant.

Karat et al[12] found that coital history was a significant risk factor with 37%in cases and 33%among controls but in our study coital history was given only by 7% of the cases and 4%

of controls. 39% cases compared to 14% controls had WBC in their vaginal fluid indicating presence of genital tract infection in Karat's study.

Ferguson and associates[100] reported that PPROM is associated with low maternal hemoglobin and low socioeconomic status. The lower hemoglobin level may be a marker for subclinical infection.

In a study conducted in Bangalore by Fathima, the risk factors in the present pregnancy were urogenital infections 15%, malpresentation 7% and cervical encerclage 4%

Cervical encerclage was present in 4% of our cases which is comparable to the study by Kamala Jayram (2%) and Coombs (3%). [100,101]

In a recent study by Ibishi et al[78], 29% percent had previous abortions and 22% were smokers and among the multiparous patients 59% experienced previous PROM.

Studies by Kilpatrick et al [103] Harger et al[96] and Ekwo et al[104]. demonstrated a twofold to fourfold increased risk for PPROM with self-reported current cigarette smoking.

Abnormal per vaginal discharge was found as a risk factor for PROM in a study done in Uganda in 2015. [105]

66% of cases had laboratory evidence of urinary tract infections at the time of admission, as compared to 5% of controls in our study.

Smoking was an important risk factor seen in 22% of PROM cases in a study by Ibishi[78] in contrast to 4% in our study.

According to a study by Shweta Patil[88], the most common risk factor was malpresentation13% followed by antecedent coitus10%, previous h/o PROM6% UTI 6%, polyhydramnios 4% and twins 2% among the PROM group. All these risk factors were lesser in the controls with statistical significance for malpresentation, coital history, previous PROM and UTI. We had similar results in our study.

	Revathi et al[106]	Shweta Patil et al[88]	Present study
Symptoms of UTI	13	6	12
Abnormal discharge p/v (lower genital tract infection)	10	-	13
Malpresentation	5	13	9
Recent coital history	-	10	7
Cervical encerclage	3	-	4
Polyhydramnios	5	4	8
Anaemia	22	-	10
Twins	-	2	-
Invasive procedures	-	-	4
Tobacco chewing/smoking	-	-	4
Early vaginal bleeding	-	-	7
GDM	-	-	2

Analysis according to AFI, WBC, CRP (table 9,10,11)

AFI

In our study, 24% of cases and 2% of controls had AFI ≤5. This difference in AFI comparison between two groups was statistically significant. This was found to be comparable to a study by Nagaria et al[107] in which 58.3% of cases and only 4.4% of controls had AFI<5cm.

The present study shows that, mean AFI of cases was 7.9 ± 5.0 and Mean AFI of controls was 11.44 ± 2.8. This difference in mean AFI between two cases was statistically significant.

Analysis from the present study (table 27) shows that in cases among those with AFI ≤5, 37.5% had Perinatal mortality,54.2% had ≤5 Apgar at 5 minutes, 45.8% had NICU admission and 62.5% had LSCS and among those with AFI >5, 0% had Perinatal mortality, 18.4% had ≤5 APGAR at 5min, 35.5% NICU admission and 46.1% had LSCS. The difference in perinatal mortality, APGAR at 5min and NICU admission between two groups of AFI was

statistically significant. Among controls significant difference was observed for LSCS between AFI ≤5 and >5.

In a similar study conducted in Brazil in 2016[108], it was observed that when AFI was less than 5cm the risk for perinatal mortality was three times higher. When AFI was <3cm, they noted double the risk of an Apgar score < 7 at 1minute and four times the risk of neonatal sepsis and early neonatal mortality.

30% of the cases underwent LSCS when AFI was <5 in a study by Shweta[76] at al which is less when compared to 62.5% in our study.

CRP

In our study significantly, more number of women among the cases had positive CRP when compared to the controls.

Xie and colleagues[109] in 2014 reported that higher CRP level before delivery and oligohydramnios at admission in women with PPROM are associated with histological chorioamnionitis.

In a study by Stepan et al[110] maternal CRP was significantly higher in women with microbial invasion of amniotic cavity and histological chorioamnionitis.

Analysis according to vaginal swab culture sensitivity (table12,13)

Among cases14 (14%) showed growth of the fungal pathogen, Candida albicans and 9(9%) showed growth of bacterial pathogens accounting for an isolation rate of 23 (23%). In contrast, among controls only 6(6%) of the swabs yielded Candida albicans and none yielded any bacterial pathogen. The difference in the isolation rate of the pathogens between the two groups was statistically significant (p=0.001). The break-up of the pathogens in the PROM group was as follows: Candida albicans 14(14%), Escherichia coli 4(4%), Pseudomonas aeruginosa 3(3%), Enterobacter species 1(1%) and Streptococcus pyogenes 1(1%).

Our study is in correlation with a study conducted in 2014 in Mangalore, Karnataka where the most common pathogen encountered was Candida species. Other organisms isolated were

Klebsiella pneumoniae, Staphylococcus aureus, Group B Streptococcus, Acinetobacter and a rare case of Streptococcus pneumonia all of which were significantly correlated with PROM.[77]

In our study normal vaginal flora was seen in 77% of cases against 94% of controls in contrast to study by Bharati and colleagues[74] (23.75% of cases and 86.25% of controls). Organisms isolated in this study were Staphylococcus aureus 20%, E.coli 13.75%, Group B Streptococci 8.75%, Enterococci 2.5% and Candida albicans 3.75% which is comparable to our study.

It is interesting to note that not only there was an increase in the presence of infective pathogens (bacterial and fungal), there was also a consequent fall of the normal flora from the genital tract.

Study	Positive culture from vaginal swab	Bacterial	Fungal
Bharathi 2013[74]	48.75	45%	3.75 (Candida albicans)
Rajarathnam 2014[77]	26.9%	12.5%	14.4% (Candida species)
Karat 2015[12]	62%	53.3%	8.7%
Milton W. Musaba 2017[86]	30%	30%	Not tested
Present study	23%	9%	14% (Candida albicans)

Mikamo and colleagues[111] found that 72.9% of patients with PPROM had bacterial vaginosis.

Risk factors such as UTI, bacterial vaginosis, Escherichia coli and Staphylococcus aureus are significantly associated with PROM. [12]

Significant association was observed between PROM cases and bacterial infections in a study conducted in 2013 in Andhra Pradesh. Staphylococcus aureus was the most common organism isolated. Bacterial vaginosis was three times more common in PROM cases than in controls.[71]

The choice of antibiotics should be based on culture and sensitivity patterns as well as epidemiological patterns. A recent Cochrane review which included 22 studies concluded that antibiotic of choice for prophylaxis in PROM is not clear.[112]
Probably the associated organisms have changed or developed resistance, hence the need to establish the current cervicovaginal bacteriology and sensitivity patterns in this population of patients.

In our hospital ceftriaxone is being used as the drug of choice for empirical treatment of cases of PROM which would effectively cover 66.6% of the bacterial pathogens according to our study and thus the practice gets validated.
Thus, Quinolones (ciprofloxacin, levofloxacin) or aminoglycosides appear to be empirical drugs which can be used to treat bacterial infections found in PROM patients. However, quinolones are contraindicated in pregnancy and our study recommends use of Aminoglycosides such as amikacin, gentamycin or Tobramycin.

In a study done in Africa, among the PROM cases, 30% of the cervicovaginal cultures were positive out of which 63% were gram positive aerobic bacteria, and only 7.5% were anaerobes. Resistance to erythromycin, ampicillin, cotrimoxazole and ceftriaxone was 44%, 95%,96% and 24% respectively. This study concluded that the spectrum of bacteria associated with PROM has not changed but resistance to the most commonly used broad spectrum antibiotics was notably high.[105]
In women with latency longer than 12hours, prophylactic antibiotics are associated with significantly lower rates of chorioamnionitis by 51% and endometritis by 88%. [59]

Women with PROM between 34 and 37 weeks might benefit from immediate delivery if they have Group B Streptococcus colonisation (seen in 14% of women). The risk of early onset neonatal sepsis in GBS-positive women was high (15.2%) when they were managed expectantly but this risk was reduced to 1.8% with immediate delivery.[113]

In our study steroids were administered to 30 % of cases and 5% of controls for fetal lung maturity. According to a few studies, A single course of betamethasone administered antenatally to patients with preterm premature rupture of membranes was associated with

decrease in frequencies of both respiratory distress syndrome and advanced grades of intraventricular hemorrhage without any increase in perinatal infectious morbidity.[114]
Some other studies report that glucocorticoids appear to diminish the beneficial effects of antibiotics in the treatment of preterm premature rupture of membranes.[114]

Analysis according to mode of delivery and indication for caesarean section (table 15,16)

This study showed 50% rate of caesarean section in the study group and 33% in the control group. This difference between two groups was statistically significant. The most common indications for caesarean section in the PROM group are fetal distress 46%, oligohydramnios 26% and failed induction 26% and in the control group are previous LSCS 30.3%, maternal desire 15.2% and others 18.2%. There was significant difference in indications such as oligohydramnios and fetal distress between cases and controls being more in the PROM group.

Mode of delivery among PROM cases in various studies

Mode of delivery	Anjana Devi[87]	Nagaraia Tripti[107]	Ibishi[78]	Shweta Ananth[79]	Shweta patil[88]	Sajida and Naushaba[115]	Present study
LSCS	45.2%	32%	28%	25%	27%	8%	50%
Vaginal Delivery	54.6%	68%	72%	75%	73%	92%	50%

The studies done by Anjana Devi, Nagaraia Tripti[107] and Vlora Ademi[78] included both term and preterm PROM cases which is similar to our study inclusion criteria.

Sajida and Naushaba[115] took into consideration only term PROM cases which is probably the reason for the very low caesarean section rate of 8% when compared to our study.

Shweta patil[88] and Shweta Anant's[79] studies included only preterm PROM cases.

In a comparative study of women with and without PPROM by Shwetha patil et al 27% of cases and 8% of controls underwent LSCS.

Swathi pandey[52] showed 31% rate of caesarean section in the study group and 12% in the control group. In the present study 50% had caesarean section in the study group and 33% in the control group.

The results from study by Ibishi[78] et al report a caesarean section rate of 28% with no statistical difference between term and preterm PROM groups.

Indication for caesarean section among PROM cases

indication	Shweta Anant[79]	Shweta patil& vikram patil[88]	Present study
Oligohydramnios	12%	0%	26%
Fetal distress	24%	51.85%	46%
Failed induction	12%	0%	26%
Previous LSCS	12%	11.11%	14%
Cord prolapse	0%	0%	4%
CPD	0%	14.80%	6%
Malpresentation	36%	22.22%	10%
Maternal desire	0%	0%	6%
Other indications	4%	0%	8%

Analysis according to maternal complications (table 17)

studies	Pandey Swathi[52]	Anjana devi[87]	Okeke[80]	Present study
Maternal morbidity	9%	21%	20%	39%

The definition of term maternal morbidity in our study comprises of factors such as clinical components such as PPH, abruption, retained placenta, puerperal pyrexia and wound infection.

Keeping this in mind the number of patients who come under this umbrella term is higher in our study. However, in other studies, the term maternal morbidity has not been adequately and specifically defined leading to discrepancies in comparison. Hence, with this in mind, the

overall conclusion is definitive that there is a relatively higher incidence of morbidity in the mothers with PROM in our study.

Maternal complications comparison between two groups

Analysis from our study showed that all the maternal complications such as puerperal pyrexia, clinical chorioamnionitis antenatally, PPH, abruption, retained placenta, foul smelling lochia and wound infection were more in the PROM group when compared to controls as seen in table 17. Among these complications, statistically significant difference between the two groups of patients was seen for clinical chorioamnionitis, puerperal pyrexia, foul smelling lochia and wound infection. The most frequent maternal complication among cases in our study was puerperal pyrexia (12%) followed by wound infection (9%) and clinical chorioamnionitis(8%).these results are consistent with observations made by Shweta Patil and Vikram Patil[88].

In the study bu Shweta patil[88], as compared to control group which showed 2% puerperal pyrexia, 11% of PROM patients had puerperal pyrexia. Chorioamnionitis 3%, wound infection 3%, urinary tract infection 2% was seen among the PROM group and none among the controls which is comparable to our study.

In a study done by Ibishi et al[78] in 2015, the most common maternal complications were chorioamnionitis, retained placenta and postpartum hemorrhage which is also similar to our study.

Maternal complications among PROM cases in various studies

Study	Clinical Chorioamnionitis	PPH	Abruption	Puerperal Pyrexia	Retained placenta	Foul smelling lochia	Wound infection
Present study	8%	6%	4%	12%	6%	4%	9%
Linehan[116]	12%	12%	18%	2.4%	21%	-	-
Shweta Anant [79]	-	1%	-	12%	-	-	1%
Shweta patil[88]	3%	-	-	11%	-	-	3%

Incidence of chorioamnionitis in various studies

Piya ray	Kodkany[117]	Linehan[116]	Swathi pandey[52]	Anjana devi[87]	Swetha patil[88]	Present study
14%	5%	12%	6%	5.6%	3%	8%

Analysis of neonatal outcome (tables 18-24)

Comparison of PROM cases according to gestational age

Gestational age in weeks	Woranart et al[118]	Kifah et al[119]	Present study
<37 (preterm PROM)	42.3%	62%	43
≥37 (term PROM)	57.69%	38%	57

Nagaria et al[107] reported low birth weight among PROM cases to be 48.5% which is comparable to 56% seen in our study.

Most of the patients with preterm PROM went into labour spontaneously or were managed actively resulting in preterm delivery whereas the control population progressed till term gestation. This is the reason for the significant difference in low birth weight between the two groups.

Analysis according to NICU admission among term PROM (≥37weeks gestation)

Study	**Number of babies admitted(percentage)**
Farhat karim[83]	43.6%
Ben chong[84]	3.6%
Present study	14%

Birth asphyxia among neonates of PROM cases in various studies

Shweta Patil[88]	Nilli[120]	Shweta Ananth[79]	present study
26%	33.3%	20%	13%

Neonatal sepsis among neonates of PROM cases in various studies

Shweta Patil[86]	Nilli[120]	Shweta Anant[79]	present study
14%	5.5%	26.7%	13%

Neonatal death among cases of PROM in various studies

Tavassoli[121]	Shweta Anant[79]	Anjana Devi[87]	Okeke[80]	Pandey Swathi[52]	Shehla Noor[122]	Sanyal MK[123]	present study
8.8%	15%	5%	8.9%	12%	12.94%	5%	5%

Analysis from some studies shows that mortality in neonates born to mothers with PROM is directly related to the duration of PROM. Nili and Shams Ansari[120] observed that neonatal mortality in patients with PROM<24hrs is less than that with >24hrs. Results from our study (table 25) show that birth asphyxia, neonatal death, still births, neonatal sepsis and intraventricular hemorrhage were more in those with PROM-delivery interval >24hrs with the later three complications showing statistical significance.

SUMMARY

The present study entitled "CLINICAL AND MICROBIOLOGICAL CORRELATES OF PREMATURE RUPTURE OF MEMBRANES AMONG PREGNANT WOMEN IN KOLAR." was conducted at R.L. Jalappa Hospital and Research Centre attached to Sri Devaraj Urs Medical College, Kolar from March 2014 to August 2015.

Based on the results of the study it can be summarized that:

- PROM can occur irrespective of the age of the pregnant woman and her parity.
- The percentage of unbooked patients among cases and controls was 22% and 11% respectively showing a significant correlation between lack of antenatal care and incidence of PROM.
- Eighty six percent of the cases and only 67% of controls fell in socioeconomic class 3 or below (middle and lower classes). This statistically significant difference suggests that lower socioeconomic status is associated with PROM.
- Women involved in strenuous physical activity were significantly at more risk for PROM compared to homemakers.
- An association was noted in this study between previous history of PROM and preterm labour with recurrence of PROM in the current pregnancy. Hence, patients with such a history may be placed under close surveillance in a tertiary care setting
- Abnormal discharge per vagina, urinary tract infection, anaemia, invasive procedures and tobacco chewing/smoking, malpresentation, early vaginal bleeding and cervical encerclage were the most common risk factors found in the study group. Thus, patients should be screened for the presence of these risk factors during routine antenatal check-up.
- A significant proportion of PROM patients had urogenital infection which is curable with proper treatment. Hence, early screening and treatment of the above complications may contribute to prevention of PROM.
- WBC count >17,000 cells/mm^3 and positive C Reactive Protein are laboratory markers of infection and were significantly more in the case population.

- There is an increased need for caesarean section which adds to the maternal morbidity among women with PROM, the most common indications being oligohydramnios, fetal distress and failed induction.
- Incidence of maternal complications such as puerperal pyrexia, wound infection, clinical chorioamnionitis, foul smelling lochia, postpartum hemorrhage and retained placenta was more in the PROM population when compared to controls which led to prolonged hospital stay and added to the morbidity.
- Increased percentage of low birth weight, low APGAR score, NICU admission, prolonged duration of NICU stay and still birth rate was noted among cases when compared to controls.
- Neonatal complications such as birth asphyxia, jaundice, neonatal sepsis and neonatal death were associated significantly with the PROM group compared to the control population.
- When the interval between onset of PROM and delivery was >24 hours, it was significantly associated with increased incidence of stillbirth, neonatal sepsis and intraventricular hemorrhage.
- Our data suggests that screening for vaginal infection if done as a part of routine antenatal examination in the 3rd trimester and if appropriate treatment measures are taken it may be possible to prevent PROM.
- Ceftriaxone effectively covers 66.6% of the bacterial pathogens according to our study. Hence the practice of using ceftriaxone for empirical treatment of patients with PROM is validated.

CONCLUSION

Our data shows that PROM tends to recur in subsequent pregnancies. This may be related to persistent etiological factors or behavioural patterns. All pregnant women should be educated regarding regular and timely antenatal check-up and special efforts should be made to identify risk factors. Hence all pregnant women should be screened for UTI, anaemia and malpresentations. Conditions such as anaemia, tobacco chewing, coitus during pregnancy, history of cervical encerclage and early vaginal bleeding should be addressed at the earliest with appropriate treatment or lifestyle modifications in those who have a past history of PROM.

A higher incidence of maternal complications such as clinical chorioamnionitis, retained placenta, postpartum hemorrhage, wound infection and puerperal pyrexia was seen among women with PROM in our study. The obstetricians should anticipate, detect and treat the above complications that may follow.

A significant association of increased neonatal morbidity was observed with PROM. This observation mandates that the obstetrician and neonatologist should work as a team to ensure optimal care for the mother and neonates born to women with PROM.

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ANNEXURES

PROFORMA

PERSONAL DETAILS:

NAME: F

AGE:

HOSPITAL NUMBER:

DATE: __/__/__

ADDRESS:

OCCUPATION:

SOCO ECONOMIC STATUS:

TELEPHONE NUMBER:

CHIEF COMPLAINTS:

G P L D A WITH _____ MONTHS OF AMENORRHOEA, APPRECIATING FETAL MOVEMENTS WELL.

H/O PV LEAK YES /NO SINCE

H/O FOUL SMELLING DISCHARGE PV YES /NO SINCE

H/O PAIN ABDOMEN YES/NO SINCE

H/O PV BLEED YES/NO SINCE

H/O FEVER YES/NO SINCE

H/O BURNING MICTURITION YES/NO SINCE

H/O COITUS 1 WEEK BEFORE YES/NO SINCE

H/O CERVICAL CIRCLAGE YES/NO SINCE

H/O AMNIOCENTESIS YES/NO SINCE

OBSTETRIC HISTORY:

MARRIED LIFE- _____ YEARS /MONTHS

CONSANGUINOUS/ NONCONSANGUINOUS

PREVIOUS H/O PRETERM LABOR/PROM/CHORIOAMNIONITIS/ABORTIONS

MENSTURAL HISTORY-

LMP-

EDD-

PERIOD OF GESTATIONAL-_____ WEEKS_____ DAYS

PAST MENSTRUAL CYCLES:

PAST HISTORY-

H/O HYPERTENSION/DIABETES/EPILEPSY/BRONCHIAL

ASTHMA/TUBERCULOSIS

H/O BLOOD TRANSFUSION

H/O PREVIOUS SURGERY

H/O SIMILAR COMPLAINTS IN THE PAST

PERSONAL HISTORY-

H/O SMOKING/ TOBACCO CHEWING YES/NO

GENERAL EXAMINATION-

PALLOR/ICTERUS/CLUBBING/CYANOSIS/EDEMA/LYMPHADENOPATHY-

PULSE RATE:

B.P :

TEMPERATURE:

BREAST/SPINE/THYROID:

SYSTEMIC EXAMINATION-

R.S-

C.V.S-

C.N.S-

PER ABDOMEN:

PER SPECULUM :

PER VAGINAL:

INVESTIGATIONS:

BASELINE CBC WITH BLOOD GROUPING TYPING.

WBC COUNT

SEROLOGY :HIV/HBSAG/VDRL.

CRP

URINE ROUTINE

URINE CULTURE SENSITIVITY

NST

OBSTETRIC ULTRASOUND.

HIGH VAGINAL SWAB CULTURE SENSITIVITY

FOLLOW UP

MATERNAL COMPLICATIONS IF ANY:
DURATION OF HOSPITAL STAY:
PROM- delivery interval

BABY DETAILS:

Live/ stillbirth/ birth trauma
Gender
Gestational age
Birth weight
Apgar score
NICU admission
Indication for NICU admission
Neonatal morbidity
Mortality
Cause of death
Duration of NICU stay

IDENTIFIED RISK FACTORS

INFORMED CONSENT

Date

I/we the patient attenders were explained the condition of the patient and the need for intervention. I/we the patient attenders of the patient agree to participate in the study. The nature and purpose of the study have been explained to us in our own understandable language. i/we understand that participation in the study is voluntary and we are free to withdraw at any time, without giving any reason, without my medical care or legal right being affected. I/we give permission for these individuals to have access to patient records, and we hereby give consent to the treating doctors for the intervention and we do not claim any responsibility on to the treating doctors, staff or hospital for any maternal and fetal complications and patient condition.

Signature of patient/attenders

KANNADA CONSENT FORM

ಮಾಹಿತಿಯುಕ್ತ ಸಮ್ಮತಿಯ ನಮೂನೆ

ಇದು ಸೂಕ್ತ ಪೂರ್ವಸೂಚಕ ಅಂಶಗಳಲ್ಲಿ ಜ್ಞಾನ ತೀವ್ರ ನಿಗಾ ಚಿಕಿತ್ಸೆಯ ಅಗತ್ಯ ಹೆಚ್ಚಿನ ಅಪಾಯ ರೋಗಿಗಳ ಆರಂಭಿಕ ಗುರುತಿನ ಉಪಯುಕ್ತ ಇರಬಹುದು ಭರವಸೆಯಿದೆ . ನೀವು ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ಒಪ್ಪುತ್ತೀರಿ ವೇಳೆ ನೀವು ಅಥವಾ ನೀವು ಅಥವಾ ಎರಡೂ ಜವಾಬ್ದಾರಿ ವ್ಯಕ್ತಿಯಿಂದ ಮಾಹಿತಿ (ಪ್ರತಿ PROFORMA ಮಾಹಿತಿ) ಸಂಗ್ರಹಿಸುತ್ತದೆ . ನಿಮ್ಮ ಆಸ್ಪತ್ರೆ ದಾಖಲೆಯಿಂದ ಚಿಕಿತ್ಸೆ ಮತ್ತು ಸೂಕ್ತ ವಿವರಗಳನ್ನು ಸಂಗ್ರಹಿಸುತ್ತದೆ . ಸಂಗ್ರಹಿಸಿದ ಈ ಮಾಹಿತಿ ಮಾತ್ರ ಪ್ರೌಢಪ್ರಬಂಧದಲ್ಲಿ ಮತ್ತು ಪ್ರಕಟಣೆ ಬಳಸಲಾಗುತ್ತದೆ . ಈ ಅಧ್ಯಯನವು ಸಾಂಸ್ಥಿಕ ನೈತಿಕ ಸಮಿತಿಯು ವಿಮರ್ಶಿಸುತ್ತದೆ ಮಾಡಲಾಗಿದೆ . ನೀವು ಭಾಗವಹಿಸಲು ಇಚ್ಛಿಸದಿದ್ದರೆ ನೀವು ಪಡೆಯುತ್ತಾನೆ ಆರೈಕೆ ಬದಲಾಗುವುದಿಲ್ಲ . ನೀವು ಸ್ವಯಂಪ್ರೇರಣೆಯಿಂದ ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ಒಪ್ಪಿಕೊಂಡಲ್ಲಿ ಹೆಬ್ಬೆಟ್ಟಿನ ಗುರುತು ಸೈನ್ / ಒದಗಿಸುವ ಅಗತ್ಯವಿದೆ .

ನಾನು ಯಾವುದೇ ಸಮಯದಲ್ಲಿ ಅಧ್ಯಯನದಿಂದ ಹಿಂತೆಗೆದುಕೊಳ್ಳುವಂತೆ ಮತ್ತು ಈ ನನ್ನ ಮುಂದಿನ ಆರೈಕೆ ಬದಲಾಗುವುದಿಲ್ಲ ಉಚಿತ ಉಳಿಯಲು ಎಂದು ಅರ್ಥ . ನಾನು ಓದಲು ಅಥವಾ ನನಗೆ ಓದಲು ಮಾಡಲಾಗಿದೆ ಮತ್ತು ಅಧ್ಯಯನದ ಉದ್ದೇಶ , ಬಳಸಲಾಗುವ ವಿಧಾನ , ಅಧ್ಯಯನ ಮತ್ತು ಅಧ್ಯಯನದ ಸಮಯದಲ್ಲಿ ಸಂಗ್ರಹಿಸಿದ ಮತ್ತು ಬಹಿರಂಗ ನಡೆಯಲಿದೆ ಮಾಹಿತಿಯನ್ನು ಪ್ರಕೃತಿಯಲ್ಲಿ ನನ್ನ ಒಳಗೊಳ್ಳುವಿಕೆ ಸಂಬಂಧಿಸಿದ ಅಪಾಯ ಮತ್ತು ಲಾಭಗಳನ್ನು ಅರ್ಥ . ನಾನು ಅಧ್ಯಯನ ಮತ್ತು ನನ್ನ ಪ್ರಶ್ನೆಗಳಿಗೆ ವಿವಿಧ ಅಂಶಗಳನ್ನು ನನ್ನ ತೃಪ್ತಿ ಉತ್ತರಿಸುವ ಬಗ್ಗೆ ನನ್ನ ಪ್ರಶ್ನೆಗಳನ್ನು ಕೇಳಲು ಅವಕಾಶ ಹೊಂದಿದ್ದರು . ನಾನು , ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ಮತ್ತು ಪ್ರೌಢಪ್ರಬಂಧದಲ್ಲಿ ನನ್ನ ವೈಯಕ್ತಿಕ ಮಾಹಿತಿಯ ಸಂಗ್ರಹಣೆ ಮತ್ತು ಡಿಸ್ಕ್ಲೋಸರ್ ಅಧಿಕೃತಗೊಳಿಸಲು ಒಪ್ಪುತ್ತೀರಿ ರುಜುಮಾಡಿರುವ .

ವಿಷಯದ ಹೆಸರು

(ಪಾಲಕರು / ಗಾರ್ಡಿಯನ್ಸ್ ಹೆಸರು)

DATE : ಸಹಿ / ಹೆಬ್ಬೆಟ್ಟಿನ ಗುರುತು

ಒಪ್ಪಿಗೆ ತೆಗೆದುಕೊಳ್ಳುವ ವ್ಯಕ್ತಿಯ ಹೆಸರು ಮತ್ತು ಸಹಿ

KEY TO MASTER CHART

- **booking status**: 1- booked, 2-unbooked
- **BMI**: 1- <18, 2- 18to 24.9, 3->25
- **Occupation**: 1-homemaker, 2- working
- Fever, foul smelling amniotic fluid, early vaginal bleeding, recent coitus, symptoms of UTI, white discharge per vagina, malpresentation, polyhydramnios, multiple pregnancy, anemia, gestational diabetes, cervical encirclage, PPH, abruption, retained placenta, puerperal pyrexia, foul smelling lochia, wound infection, birth asphyxia, jaundice, neonatal sepsis, intraventricular haemorrhage, stillbirth, neonatal death: 0- absent, 1- present.

- Past history of abortion, previous PROM, previous preterm birth: 0-absent 1-present, N-not applicable (for primigravidas)

- **Mode of delivery**: 1-vaginal, 2- caesarean
- **Indications for caesarean section**: oligohydramnios, fetal distress, failed induction, previous LSCS, cord prolapse, CPD, malpresentation, maternal desire: N- not applicable (for vaginal deliveries), 0- not an indication, 1- indication for caesarean
- **Apgar score**: 1- <5, 2- ≥5
- **NICU admission**: 0- not admitted, 1- admitted
- **Swab culture**: 1-normal vaginal flora, 2-fungal, 3-bacterial